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PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS. ANNUAL SUBSCRIPTION, $10.00

Entered as Second Class Matter Feb. 7, 1929, at the Postoffice at Chicago, Under the Act of Congress of March 3, 1879

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VOLUME 40 (old series Volume 97) AUGUST 1948 NUMBER 2

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1949

NECROSIS OF INTRAOCULAR TISSUES

BERNARD SAMUELS, M.D.
NEW YORK

IN TEXTBOOKS on general pathology, considerable space is devoted to the study of the death of tissues. However, in the teaching of the special pathology of the eye, disease from this standpoint fails to receive the attention that its frequency and extent warrant.

In accordance with the nomenclature of general pathology, the term necrosis means the local death of cells or of tissues in an organ, notwithstanding the loss of which the organ as a whole continues to live.

Intimately associated with necrosis are the conditions of degeneration, atrophy and gangrene. Degeneration signifies an alteration in the metabolism of the cells that compose a tissue, but not to such an extent as actually to cause the death of the cells. Atrophy means acquired diminution in the size of cells or of tissues after maturity has been attained. Degenerated or atrophic tissue may be converted into necrotic tissue. Gangrene signifies necrosis but only that following an invasion of saprophytic organisms.

In ocular pathology the term necrosis is employed in a narrow sense, referring, unless otherwise qualified, to the death of the cells of a tissue, it being understood that the framework is spared and is capable of being resuscitated by the ingrowth of cells from the adjacent living tissue. For example, a piece of cornea, excised for the purpose of transplantation, may lose its corpuscles and remain in a state of necrosis until corpuscles in the receiving cornea have had time to divide and migrate into the graft.

Bearing in mind that knowledge is progressive, the present observations, based on a study of over 800 globes that showed necrotic tissue under the microscope, may be considered as a continuation, on a wider scale, of observations on intraocular necroses in two papers published in 1929 [1] and 1933.

There are two types of intraocular necrosis, namely, the noninflammatory and the inflammatory type.

From the Eno Laboratory of the New York Eye and Ear Infirmary.

Delivered as the deSchweinitz Lecture before the Section of Ophthalmology of the College of Physicians of Philadelphia, Nov. 20, 1947.

1. Samuels, B.: Necrosis of the Iris, Tr. Ophth. Soc. U. Kingdom **49**:421-436, 1929; A Study of the Anatomic and Clinical Manifestations of Necrosis in Eighty-Four Cases of Choroidal Sarcomas, ibid. **53**:520-570, 1933.

NONINFLAMMATORY TYPE

NECROSIS CAUSED BY CIRCULATORY DISTURBANCE

Iridodialysis.—The purest form of intraocular necrosis is that which is produced when the arteries, veins and nerves of the iris are suddenly and completely severed from their connection with the ciliary body. Usually the dialysis takes place in no more than a sector of the iris and then the actual necrosis is confined to the ciliary zone. The corresponding pupillary sector remains intact because its nutrition is maintained from the collateral circulation by way of the lesser arterial circle of the iris. Iridodialysis is commonly the result of injury, accidental or surgical; but it may be caused, very slowly it is true, by the extension of a malignant melanoma of the ciliary body into the anterior chamber, or,

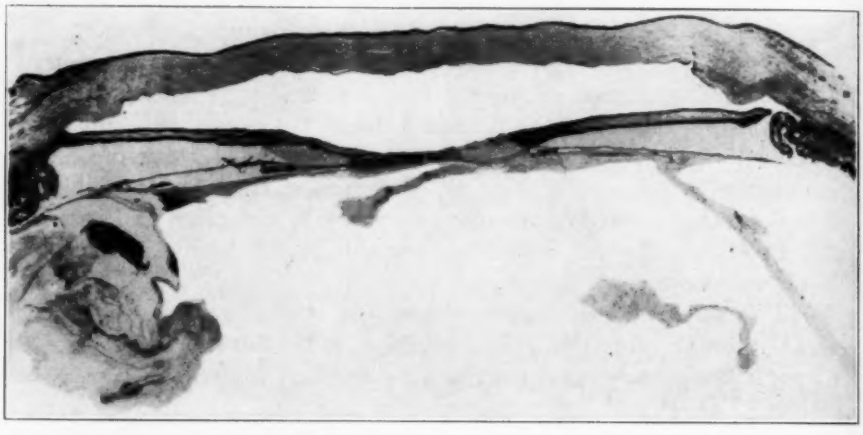

Fig. 1.—Slow necrosis of the iris on the right side due to dialysis; atrophy on the left side resulting from peripheral anterior synechia. The homogeneous and slightly edematous stroma, with a pocket of pigment granules at either end, characterized the necrosis.

rarest of all, it may be spontaneous. The sector is thrown into shallow folds and the pupillary border is drawn in by the contraction of the sphincter muscle. The nuclear elements disappear from the stroma, seemingly one at a time. A few pale strands in a rarified matrix are all that is left of the walls of the blood vessels. For a long time no perceptible change takes place in the pigment epithelium, and then it only becomes thinner, as does the whole iris (fig. 1).

Cyclodialysis.—What happens to the ciliary muscle when the anterior ciliary arteries are severed was shown in 2 globes in which cyclodialysis occurred on one side. The corresponding part of the muscle was necrotic, whereas on the other side it was normal. In contrast to the necrotic part of the muscle, the ciliary processes and the iris were everywhere normal.

In 1 globe the long posterior ciliary artery and nerve had been severed on one side by a perforating wound back of the ora serrata. The iris and the ciliary processes on this side were totally necrotic, whereas elsewhere they were not affected and everywhere the ciliary muscle was normal. A similar necrosis would be produced by coagulation during diathermy should the artery and nerve be brought into the field of the puncture.

Glaucoma.—By far the greatest number of eyes studied showed evidences of glaucoma, since the conditions in which glaucoma plays a role are manifold. In glaucoma, no structure of the eyeball escapes damage, but the iris and the ciliary processes are the only ones that may be actually necrosed. In chronic simple glaucoma, atrophy of the iris is induced by the gradual arrest of the blood supply. In acute fulminating glaucoma, circulatory necrosis of the iris is induced by the sudden cutting off of the circulation. The length of time that any tissue is able to survive after the complete arrest of its blood supply varies, some tissues having greater power of survival than others. It is certain that the survival period of the delicate stroma of the iris is relatively brief, since partial or complete necrosis may follow the shortest attack of fulminating glaucoma. The pupillary zone of the iris is the part that is apt to be the most severely damaged, probably because the circulation is not so active as in the zone nearer the greater arterial circle. Hemorrhages are seldom seen with glaucomatous necrosis of the iris because the afferent and efferent vessels are blocked at the same moment (fig. 2).

In glaucoma the necrosis of the ciliary processes often coincides with that of the iris. It may be confined to the low cells of the apexes, or it may include some of the stroma. Necrosis of the ciliary processes may account for the sudden reduction of tension following a severe acute attack of glaucoma. The tension may remain low, probably because the processes are necrotic and cannot secrete the normal amount of aqueous.

Finally, in acute glaucoma not all the cornea is affected in the same way. Absence of corpuscles in the posterior central third, where the lymph flow must be more sluggish than at the base, is usual.

INFLAMMATORY TYPE

NECROSIS CAUSED BY PYOGENIC BACTERIA

Inseparably connected with necroses of intraocular tissues are deleterious, diffusible substances, generally and vaguely called toxins. No agent is more destructive to the inner layers of the eye than the toxins derived from pyogenic bacteria. Within the tissues themselves, after they have been rendered dead by circulatory disturbance or by

bacteria, secondary toxins develop which are capable of damaging the surviving parts to an extreme degree.

Bacteria Ectogenously Located (in the Cornea).—The cornea, because of its avascularity and accessibility, is the most favorable site in the entire body for the local effects of bacterial toxins. Axenfeld and Uhthoff, in 1896, discovered that the pneumococcus is the cause of the typical ulcus serpens of the cornea. The layers of the inner portion of the eye are proverbially sensitive, as is shown by the irritation following the irrigation of the anterior chamber with a solution too cold or, worse still, too warm, or with one the ingredients of which are not in exactly

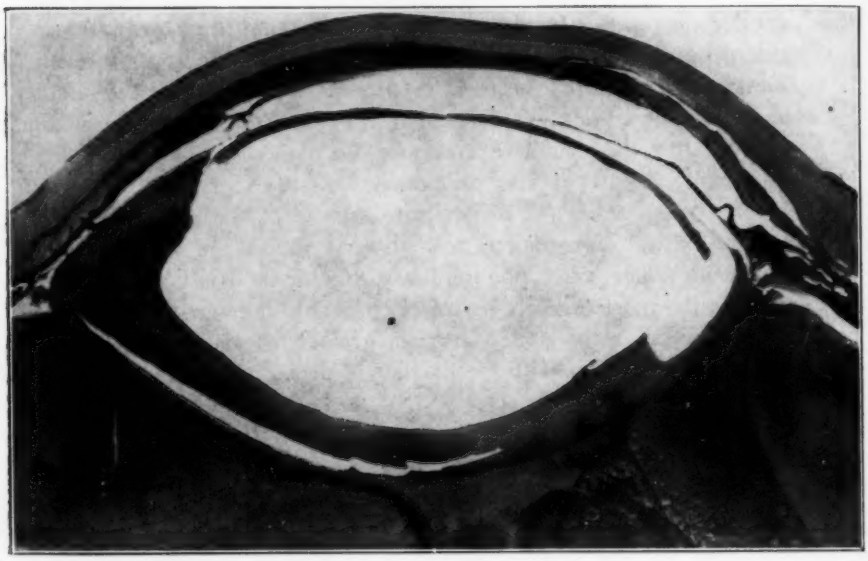

Fig. 2.—Malignant melanoma of the choroid. The necrosis of the iris and of the posterior middle layers of the cornea is due to the pressing forward of the lens, and not directly to the tumor. Blood vessels in the iris appear as streaks parallel to the surface in a homogeneous matrix.

the right proportions. The toxins from a serpiginous ulcer diffuse into the aqueous, probably in extraordinarily small quantities. Nevertheless, they are able to set up a condition of intoxication, pure and simple, and profound enough to cause necrosis of the iris and hyperemia of the blood vessels of the ciliary processes and, to a less extent, those of the retina. The necrotic iris may be so swollen and edematous as to attain twice its normal thickness. Because of the loss of its nuclear elements, the stroma takes on a characteristic ghostlike appearance, in the midst of which hyalinized walls of vessels filled with blood are often seen. Owing to the diluting effect of the flowing blood, the endothelial lining of the vessels is preserved. The sphincter muscle, being resistant, may be

present on one side and absent on the other. The pupillary zone is the part most affected, just as it was noted to be in necrosis from circulatory disturbance. Then, too, the pupillary zone is thin, and it is through its sharply pointed opening that toxins must pass on their way to the posterior chamber.

When toxins come from the cornea, the stroma of the iris affords a certain amount of protection to the pigment epithelium lining its posterior surface except at the pupillary margin, where the two rows of pigmented cells bend forward over the sphincter muscle. These particular cells react by swelling, bursting and setting free their pigment granules. This they do, albeit far more slowly, in cases of low grade uveitis and in extreme old age. The first effect of the toxins as they attack the pigmented cells on the posterior surface of the iris is to dissolve the cement substance that binds the cells together, whereupon the cells, free from tension, lose their tall pyramidal shape and become round. As a still more striking pathologic feat, they take on the power of locomotion, often wandering forward into the iris, singly or in groups, as though to find refuge from danger. In this way, in necrosis of the iris in its recent state three orders of round pigmented cells are to be differentiated in the stroma (fig. 3). The normal clump cells are recognized by their intimate relation to the sphincter muscle. The chromatophores draw in their processes and become rod shaped or round. They are the least pigmented of all. The intensely black cells are those from the pigment epithelium, and these may make their way forward into the anterior chamber.

From an anatomic point of view, the ciliary processes are particularly susceptible to toxins. They are thin, and the two epithelial layers that cover their apexes are composed of low cells; moreover, the pigmented row is lightly pigmented. In the most virulent cases of corneal ulcer, the ciliary processes may become necrotic concomitantly with the iris.

The reaction of the iris to the toxins arranges itself in two stages, a fact which explains the long-lasting irritability of the eye after the corneal lesion has healed. In the first stage the reaction is directed against the primary toxins from the pyogenic bacteria. It is marked, as stated, by necrosis of the stroma and by the formation of a hypopyon, many of the cells of which have migrated from the ciliary processes. The character of a hypopyon varies. It contains mostly pus cells, with more or less fibrin, to which are added desquamated endothelial cells and occasionally blood. The reaction is cumulative, increasing in intensity as long as the bacteria live. In the second stage, which sets in as soon as the bacteria die, the reaction is directed against the secondary toxins which emanate from the dead portion of the iris and from the necrotic hypopyon. Myriads of fresh polymorphonuclear leukocytes migrate

from the parts that have been saved into the necrotic iris and hypopyon to start the process of organization. The general surgeon recognizes the toxic action of dead pus and takes precautions against its accumu-

Fig. 3.—Traumatic necrosis of the iris in the earliest stage. The pupillary zone is edematous and appears ghostlike. The pigmented cells are of three orders —clump cells, chromatophores and cells from the pigment layer.

lation by means of posture and irrigation. Acting on the same principle, the ophthalmic surgeon in treating a corneal ulcer, when the hypopyon is excessive, opens the chamber and removes the hypopyon in order to shorten the reaction.

That a necrotic iris is in itself noxious was proved in a study of several globes of the series in which the epithelium of the lens was killed in a stretch corresponding exactly to that occupied by the overlying adherent necrotic iris, whereas, in contrast, in the exposed pupillary area the epithelium remained normal. The organization of a necrotic iris takes place with great rapidity, and the contraction may be so extensive that the structure may be reduced to a dense vascular stump in the angle. The disappearance of a sector of the iris into the angle within a few days after a cataract extraction with round pupil is too rapid for atrophy—most likely it is necrosis (fig. 4). In the edematous phase a necrotic elevated sector of the iris would be too pulpy to be seized with

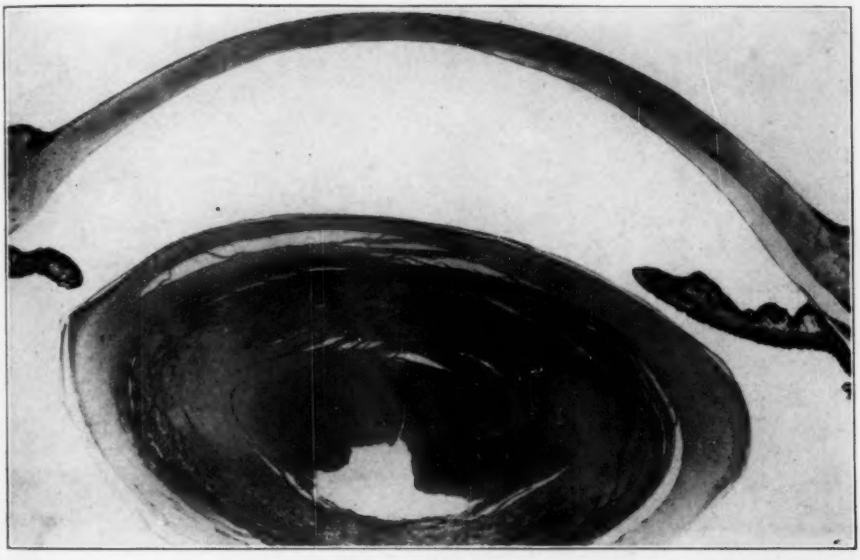

Fig. 4.—To the left, a very cellular and vascular stroma, after necrosis with organization, bears no resemblance to the original structure.

the forceps, whereas an atrophic sector could be picked up—and it is surprising how much resistance an atrophic iris may offer to traction.

Bacteria Endogenously Located.—(*a*) In the Anterior Chamber: When the bacteria are lodged within the anterior chamber, an infection is set up, in contradistinction to an intoxication, when the bacteria work from the cornea. Attacking the cornea from the chamber side, the bacteria first produce the disappearance of the endothelium on Descemet's membrane and of the corpuscles between the lamellas of the posterior third of the cornea.

The infection in the anterior chamber may attain such force that it not only kills the corpuscles but coagulates the lamellas, causing them to

fuse in one swollen opaque, homogeneous layer. Generally the most anterior lamellas, together with Bowman's membrane and the epithelial covering, escape, no doubt owing to the greater distance from the origin of the toxins and to the diluting effect of the flowing conjunctival secretion.

Every totally necrotic area, no matter where it is, may be considered an irritating foreign body. Hence the reaction to a dead cornea is of

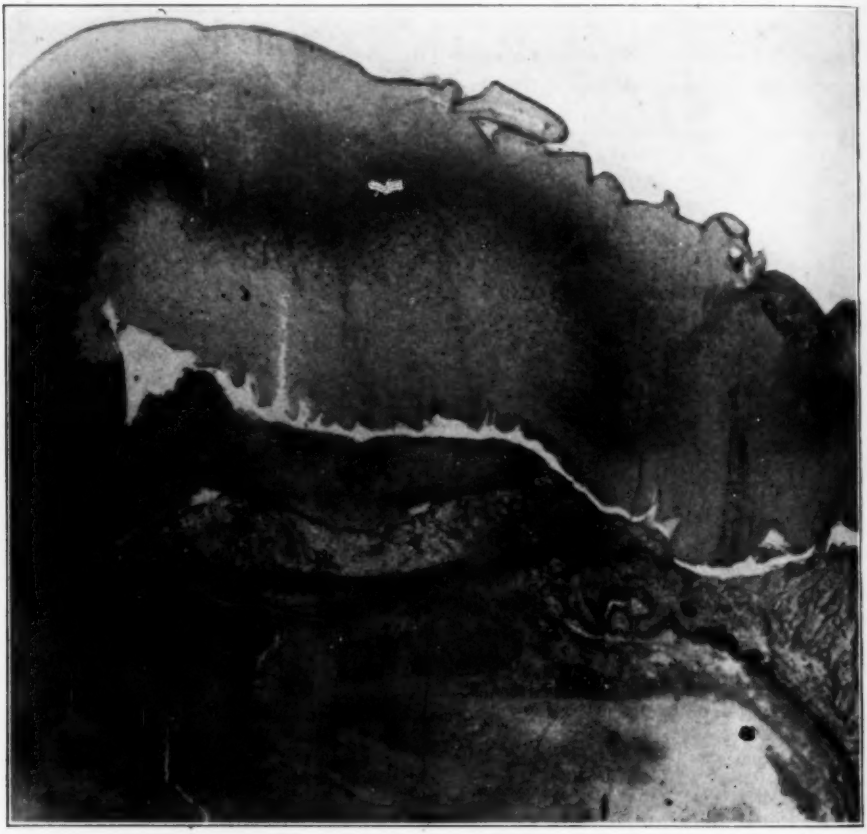

Fig. 5.—The cornea is swollen to twice its normal thickness. In the posterior layers both nuclei and lamellas are dead, as as a result of toxins from the anterior chamber. To the right there is a collection of pus cells (ring abscess). The iris is necrotic, but the pigment epithelium, being protected by the stroma, is remarkably well preserved.

the nature of a demarcating process, distinguished by the migration of countless leukocytes into the periphery of the cornea, forming a swollen, yellowish wreath; whence comes the name "ring abscess" (fig. 5). The leukocytes are prevented from entering the slough by the negative chemotactic action of the secondary toxins therein generated. However, they

aid in the liquefaction of the partially necrotic lamellas that bind the dead to the living tissue, so that the former may be expelled. It is said that leukocytes will attack tissue only after it has been damaged and that there is no evidence that they will attack normal tissue, a fact which explains the return to normal of a broad, swollen, yellowish gray zone that surrounds a corneal ulcer.

In all cases of toxins in the aqueous the condition of the angle of the anterior chamber is to be taken into account. When the angle is open, the outflowing aqueous takes care of toxins for a certain time. When the angle is blocked, the concentration of the toxins starts from the beginning.

(*b*) In the Vitreous Body: 1. Endophthalmitis septica. When an infection is confined to the anterior chamber, there is hope for the retention of the eye. When the bacteria are located in the posterior chamber or in the vitreous body, the prognosis is invariably bad because of the involvement of the ciliary body. In the earliest days of bacteriology it was thought that the virulence of pyogenic bacteria was due to the disturbance in the vital processes of their host by the mere mechanical effect of their presence. The extreme minuteness of pyogenic cocci may be inferred from the fact that eight to ten may be strewn across one red blood cell. In the laboratory, colonies of bacteria are seldom found in the slides of eyes that have been removed because of infection. The bacteria that induce the ordinary intraocular infection seem to be short lived. It used to be taught that bacteria kill a tissue by robbing it of substances necessary to its metabolism. It is true that bacteria do derive their food from their host, but it is by means of the toxins into which this food is converted that the harm is done.

Bacteria lodged within the vitreous body, as elsewhere, require a certain period for multiplication and evolution before they can create toxins. The latter irritate the ciliary body and retina and call forth the migration of pus cells toward the bacteria in the vitreous, where they localize to form an abscess. This inflammatory process is known as endophthalmitis septica. This is the mildest form of infection of the vitreous, so mild that the delicate, highly organized retina is not destroyed. The leukocytes come mostly from the very vascular ciliary processes and in less amount from the less vascular retina. The abscess soon becomes necrotic and of itself irritating, as occurs with a hypopyon. The first steps in the organization of the dead mass come from the ciliary body, on which account the detachment of the retina begins anteriorly. The detachment is the principal cause of the loss of vision. The essential feature in endophthalmitis septica (abscess of the vitreous) is the preservation of the inner layers of the eye, the loss of cells being no greater than in an ordinary inflammatory process.

2. Panophthalmitis septica. This condition is characterized by total and widespread tissue death. No part of the eye escapes. When the primary seat of the infection is in the vitreous, the first layer to be destroyed is the retina, opening the way for the bacteria to attack and destroy the choroid by suppuration. The infection spreads through the sclera into the space of Tenon, setting up an orbital cellulitis, with its clinical entity of chemosis of the conjunctiva, exophthalmos and immobility of the eye. The essential feature of panophthalmitis septica is what may be termed universal tissue death.

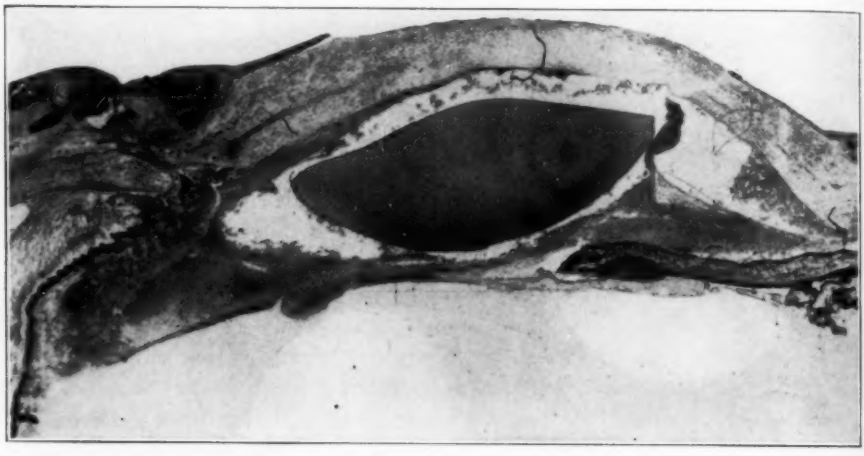

Fig. 6.—To the left, tags of iris are seen in the wound. The cornea here is replaced by thin, wavy bundles of connective tissue. The central lamellas are devoid of nuclei, and the iris is necrotic. A pocket of necrotic cells of the pigment layer lies in the pupillary zone. The sharply defined nucleus, surrounded by a phagocytic zone, is somewhat displaced by artefact.

NECROSIS CAUSED BY THE RETENTION OF LENS MATTER

The necrotizing effect on the iris and cornea of a large amount of lens matter, particularly the nucleus, retained in the anterior chamber, is strikingly like that caused by colonies of bacteria in the same location. The onset of reaction to the toxins emanating from the necrotic material is more retarded but it is cumulative until the material has been absorbed or entirely encapsulated. The increasing intensity of the reaction may be judged from the study of the case of a man aged 74 on whose eye, six weeks before enucleation, an attempt had been made to extract the lens. Clinically, the cornea was swollen and completely opaque. There was excessive chemosis of the conjunctiva, accompanied with excruciating pain. A diagnosis of panophthalmitis septica was made. Microscopically (fig. 6), a hard nucleus, entirely surrounded by a zone of phogocytes,

lay against the cornea. It had produced complete destruction of the cornea, so far as it touched it, and the replacement of the normal lamellas with ordinary wavy connective tissue. The presence of light perception and the absence of exophthalmos should have spoken against the diagnosis of panophthalmitis. A small, circumscribed, grayish defect in the stroma of the iris sometimes marks the site once occupied by a portion of lens substance that had been slowly absorbed. Small areas of necrosis cause little reaction.

NECROSIS CAUSED BY TRAUMA

Immediate and final tissue death is exemplified by the damage inflicted on the cornea by heat arising from splashes of hot metal or by chemical reaction produced by strong acids. Inflammatory toxic reactive processes come into play, the object of which is to get rid of the dead irritating tissue and to repair the part. The general principles involved in eliminating the dead material are exactly the same as those operative if death had been caused by circulatory disturbance or by the action of bacteria, instead of by direct injury.

In cases of corneal scars from caustics, it is not easy to estimate the damage that has been done to the inner structures at the moment of the accident, or afterward, by the absorption of toxins from the sloughing surface. In a case of lime burn in the present series that had long been quiescent, light perception and projection were prompt; an attempt, therefore, was made to improve vision by stripping off a membrane that was believed to lie lightly over the cornea. Owing to postoperative inflammation, the eye was enucleated. The cornea in almost its entire thickness was replaced with scar tissue, and the anterior chamber was partly occupied by an organized exudate. The iris was necrosed. The entire field was sealed off by a cataractous lens and a cyclitic membrane, leaving the posterior part of the eye normal and accounting for the retention of some sight.

Since the cornea is thick and resistant and the eye is supported by a cushion of fat in the orbit, it is seldom ruptured by a blow. The cornea may, however, be severely crushed by the direct action of a blow. In a case of this kind in the series, in which the injury was due to contusion, both corpuscles and lamellas in the middle layers of the cornea had been completely destroyed. The clinical effect was that of disciform keratitis from infection. After an inflammatory reaction of long duration, the dead mass in the cornea was liquefied and absorbed, being replaced by thin, wavy bundles of ordinary connective tissue, traversed by deep blood vessels. A cellular membrane lined the chamber side of the cornea. The iris was partially necrotic and densely infiltrated, apparently as a result of intoxication from the cornea, rather than of injury.

The reactions offered by different tissues to blows were shown in a case in which a sector of the iris had been dialyzed by a blow and yet there was no change in the cornea. Another case was informative as showing that the irregular white spots seen in the fundus after a severe contusion of the globe may not be the naked sclera. In this instance a thin band of avascular connective tissue lay over the sclera, replacing the area in the choroid and retina which had been necrosed by the contusion. Organization of a necrotic matrix proceeds rapidly in the choroid because this coat is very vascular and is protected on one side by the sclera. In a case of complete rupture of the choroid it is probably the naked sclera that is seen clinically.

In the study of the cases of prolapse of the uvea it was brought out that whenever the prolapse is covered with conjunctiva, no matter how constricted is the neck or how long the prolapse has existed, it is seldom necrosed. However, when the prolapse lies uncovered in the cornea, it quickly dies. Sloughed material is an excellent pabulum for bacteria. In my experience, prolapsed uvea in the cornea is particularly dangerous for the development of sympathetic ophthalmia.

NEUROPATHIC NECROSIS

To cite a familiar example, neurokeratitis paralytica, it was believed that section of the trigeminus nerve or excision of the gasserian ganglion leads to necrosis of the epithelium of the cornea. It is now known that there is no actual death of the epithelial cells but that the loss of control over their metabolism exercised by the sensory fibers of the trigeminus nerve merely reduces their vitality and renders them less able to withstand mechanical injury or changing atmospheric conditions. The cornea maintains itself as long as it is protected by closure of the lids.

Acute Neuropathic Necrosis of the Uvea.—1. Herpes of the Iris: It is established that herpes zoster is a specific, self-limited, unilateral inflammatory disease, caused by a filtrable virus. In herpes zoster ophthalmicus the usual primary site of the lesion is said to be in the gasserian ganglion. A few cases of herpetic iritis have been reported in which a heavy inflammatory infiltration was observed in the sheaths of the posterior ciliary nerves near the optic nerve. These nerves lose their sheaths in the emissaria, so that almost naked, flattened nerve fibers descend in the perichoroidal space. It is, therefore, surmised that at all events the virus passes toward the periphery along the nerve fibers. But it is another question as to the way in which the diseased nerve fibers produce tissue death. One theory is that chemical changes, having destructive powers, take place in the nerve endings. It is certain that mere section of the trigeminus nerve does not produce an inflammatory reaction in the uvea, in the absence of inflammation in the nerve itself.

Herpes of the iris is characterized by eruptive, circumscribed, reddish elevations on the surface of the iris, similar to those on the skin, and in very severe cases accompanied with hyphema. When the iritic eruptions are concurrent with those on the skin and cornea, there is never a question as to the diagnosis. But herpetic iritis may occur alone, without any scars on the skin or cornea. The pathologic picture, in fresh eruptions, is more typical than the clinical. It is distinguished by the excessive amount of necrosis in the stroma of the iris, identical with the inflammatory toxic type of necrosis produced by pyogenic bacteria. The reaction takes the form of a heavy plastic iridocyclitis, often with precipitates on the cornea. In the end each eruptive focus is replaced by connective tissue. Doubtless, there are cases of herpetic iritis which are not clinically typical, just as there are cases of herpetic keratitis in which the diagnosis can be made only by the concurrent typical lesions in the skin. Many eyes are enucleated because of a diagnosis of intractable iridocyclitis which came on suddenly, was unilateral and for which no cause could be found. In some of these cases the iritis is possibly of neuropathic origin, although the anatomic examination may throw little light on the cause, because secondary changes soon obscure the primary necrosis produced by the virus.

2. Acute Primary Necrosis of the Uvea: Cases have been reported in which the necrosis of the iris and ciliary body has come to anatomic examination in the fresh state, uncomplicated as yet by any signs of reaction. As in these cases bacteria, glaucoma and trauma, in short, all the conditions that are known to produce necrosis, are excluded, clinically and pathologically, the condition has come to be known as acute primary necrosis of the uvea (fig. 7).

NECROSIS OF MALIGNANT MELANOMA OF THE CHOROID CAUSING NECROSES OF PREEXISTING TISSUES

It is difficult to be original in discussing any phase of the life of intraocular tumors, for this subject was covered in detail by the elder Fuchs, on whose exact studies, chiefly cellular, the pathology of the eye has largely been developed. There is nothing singular in the spontaneous death of an intraocular malignant melanoma, since such is the common fate of all neoplasms. However, to the oculist the death of a malignant melanoma of the choroid is of prime importance, for toxins from this source may set up an extremely flagrant iridocyclitis, combined with the highest tension, creating a picture difficult to distinguish from that of the ordinary acute fulminating glaucoma. The toxins derived from necrosis of a malignant melanoma, although of tissue origin, may be fully as destructive as those elaborated by virulent pyogenic bacteria, as in panophthalmitis. It is singular that the toxins from a melanoma seem

to be more destructive than those from a retinoblastoma, which is largely necrotic from the start. A melanoma may grow to fill the vitreous cavity and yet cause neither increase of tension nor inflammatory reaction. It grows slowly, replacing structures by pressure atrophy. Its presence is not the direct cause of glaucoma. This is brought about by pressure of the subretinal fluid, which, being greater than that of the vitreous, pushes the lens forward. The largest tumor causes no inflammatory reaction so long as it is not necrotic. A necrotic mass in a tumor means totally dead material, including fibrous and cellular elements.

Necrosis of the Tumor.—1. Relation to Its Size and Shape and the Type of Cells: As with other tumors, the larger the melanoma the more apt it is to become necrotic; nevertheless, this may happen when it is

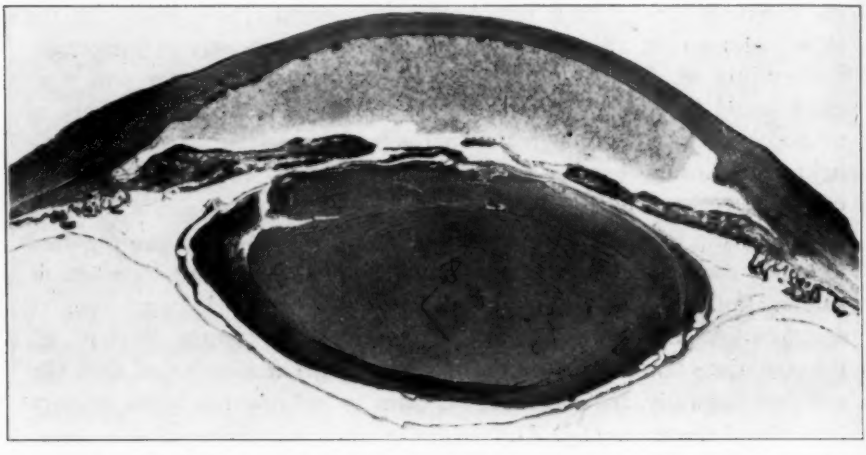

Fig. 7.—Unilateral plastic iritis with deposits on Descemet's membrane. The iris is in the inflammatory stage of necrosis. Note the loss of substance in the central area to the left and the dispersion of the pigment epithelium. As no clinical or pathologic cause could be found, the condition was called acute primary necrosis of the iris.

no larger than a cherry seed. The blood vessels of the tumor are continuous with those in the host. The cells farthest from the blood vessels, which are generally mere endothelial tubes, are the first to perish. It is not understood why a tumor which hitherto has shown no signs of tissue death suddenly becomes necrotic throughout. Most tumors are composed of different types of cells, spindle cells being in one part, round cells in another. In the matter of necrosis, the type of cell seems to make little difference. A mushroom-shaped tumor is more apt to necrose than a flat, infiltrating one, and the head of the tumor is the most often affected, as is the case with any pedunculated growth.

2. Location of the Dead Mass Within the Tumor: Groups of dead cells are encountered in almost every melanoma. They produce no

reaction; neither do larger areas, provided they are nowhere near the surface. In some tumors bands of connective tissue surround necrotic areas, indicating that a process of decay and repair has gone on at intervals. Most melanomas are located in the posterior half of the choroid; but it is chiefly on the structures in the anterior half of the eye that their necrotic action is directed.

Fig. 8.—A necrotic base of a malignant melanoma has partially destroyed the sclera and produced an inflammatory membrane, replacing the space of Tenon.

Necrosis of Preexisting Tissues.—1. Necrosis of the Sclera: In a case of mushroom-shaped melanoma the necrosis took place at the base of the tumor, directly in touch with the sclera (fig. 8). So concentrated were the toxins that the sclera was replaced by pus, which discharged itself into the space of Tenon. The type of pus from tissue necrosis is referred to as "unnatural" pus, in contradistinction to "natural" pus

from bacteria. In a case of this kind there is no immediate danger of the tumor finding its way out by the defect in the sclera, because the death of that part of the tumor antedates the defect and is the cause of it. If a fresh growth of cells should ever reach the defect, it would have to break through a thick cicatricial membrane before it could invade the orbit.

2. Necrosis of the Choroid: Although a melanoma originates within the choroid, the normal part of the choroid is the least likely of all the layers of the eye to undergo necrosis. Necrosis at the base of a melanoma is prevented from extending into the adjacent choroid because of its rich blood supply. When the retina is completely detached, toxins from a necrotic area in the inner layers of the tumor, in order to reach the choroid, must pass through the subretinal fluid and, in doing so, be diluted. On its inner surface the choroid is protected from irritating substances by the pigment epithelium, the lamina basalis (vitrea) and the choriocapillaris, and on its outer surface it is protected by the sclera. In response to extremely virulent toxins, the cells of the pigment epithelium fall away from one another, as in the iris, become round and, in order to find room, mount in groups over the lamina basalis. Sometimes a row of dead cells is detached from the smooth surface of the lamina as a result of serum derived from the choroid. A membrane or the retina adhering to the tumor serves to hold toxins back. In 1 case a membrane over a necrotic area on the anterior surface of the head of a mushroom-shaped tumor saved the overlying ciliary body and iris, while, at the same time, the opposite structures showed necrosis.

3. Necrosis of the Retina: Death is the only way by which the highly organized retina can react to virulent toxins. It literally falls to pieces. In lowly connective tissue the nuclei are the first to disappear, but in the highly organized retina the frail supporting fibers go first. The nuclei, although dead, can be identified for some time floating about in the fluid vitreous. A particularly vulnerable part of the retina, in all circumstances, is at the ora serrata, where it is faded away, leaving the rest of the retina to fall back on its inner surface.

4. Necrosis of the Papilla: In some cases of the series the papilla was deeply excavated, but seldom to the extent seen in chronic simple glaucoma. A pathologic excavation and peripheral anterior synechia make it clear that glaucoma has antedated the necrosis. In the severest cases of tumor necrosis the papilla may be converted into an indefinite, weblike groundwork lying over the lamina cribrosa, beyond which an inflammatory reaction can be traced along the blood vessels. Pigment granules may be observed far back along the inner surface of the pial sheath. The granules have their origin in the bursting of cells of the

pigment epithelium of the choroid and are carried into the nerve in the bodies of phagocytes. They are not to be mistaken for tumor cells.

5. Necrosis of the Ciliary Body: Not all parts of the inner surface of the ciliary body are affected equally by toxins. The best preserved cells are in the deep recesses of the ciliary valleys, out of the way of the poisonous currents. Attacked by concentrated toxins, the nonpigmented layer disappears completely. Owing to the surface indentations into which the cells of the pigment layer dip, this layer is not detached as readily as is the corresponding layer on the smooth and even lamina basalis of the choroid. In very severe cases of tumor necrosis the stroma of the ciliary processes is destroyed, leaving loops of congested blood vessels projecting naked into the circumlental space. The circular bundles of the ciliary muscle are often partially missing, but the longitudinal bundles are seldom much affected. In only 1 instance in the entire series was the ciliary body totally destroyed, and the nuclei of the sclera were missing as far as its external surface.

6. Necrosis of the Iris: As with the ciliary body, it is the rule for the side of the iris next the tumor to be the more affected. It is convenient here to mention a point of clinical diagnostic value: The episcleral blood vessels over a tumor are likely to be dilated, in comparison with those of the other side. The thick pigment epithelium of the iris and the dilator muscle protect the stroma of the iris from toxins coming in this direction, in the same manner in which the stroma protects these layers when the toxins attack from in front.

The damage done to the preexisting tissues as a whole corresponds in general with the size of the necrotic tumor. In 1 case a large posterior tumor had suddenly become necrotic, and simultaneously the eye showed universal necrosis. The lens had fallen back so that the iris and cornea were attacked through an open route, in full force, and sudden death was meted out to both. In the iris some of the chromatophores had no time to gather in their processes, and they, with the columnar cells of the pigment epithelium, were struck dead in their normal place and shape. The endothelium of the cornea vanished, as did the corneal corpuscles, the lamellas taking on a homogeneous aspect, as in "ring abscess" (fig. 9).

7. Necrosis of the Vitreous and Zonule: In any extensive necrosis of the uveal tract there seldom remains more than a vestige of the vitreous and zonule. These structures, together with the cement substance between the cells of the pigment epithelium, seem to have no resistance.

8. Necroses of the Lens: Invariably, the lens capsule was distended. The interval between the onset of the necrosis and the removal of the eye is too short for the formation of an anterior polar cataract. Only one such cataract was found and this was of great interest because the tumor

showed healed foci of necrosis which had probably set up a quiet attack of iridocyclitis from time to time. The lens was dead in every sense (fig. 10).

REACTION AND HEALING

Dead tissues are in themselves not capable of response. The violent inflammation and intractable pain set in, not at the moment of the necrosis, but later, after the toxins have had time to diffuse through the sclera and arrive on its surface in a diluted form. It is the reaction in the episcleral and orbital tissues that manifests itself clinically. Within

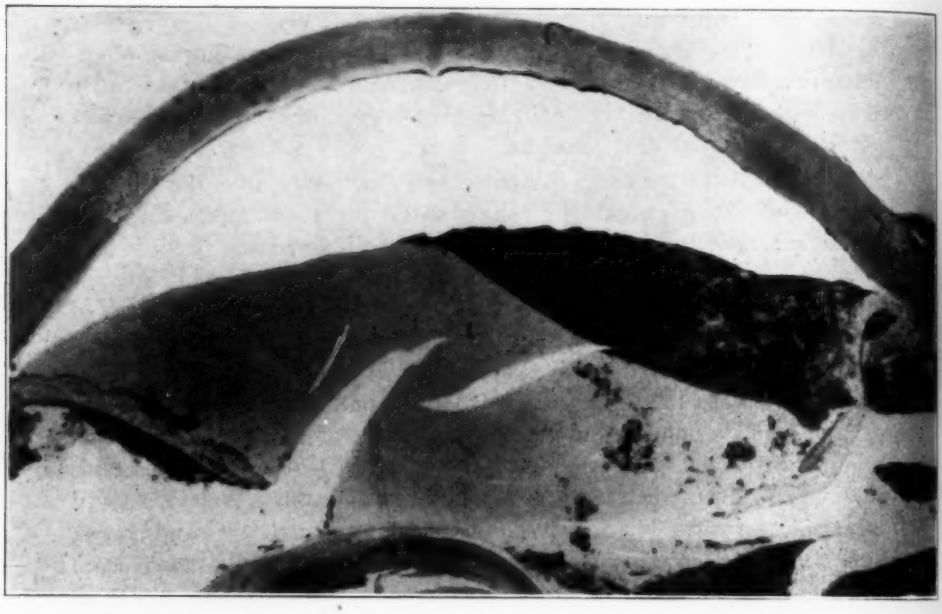

Fig. 9.—Necrosis of a large malignant melanoma of the choroid. The posterior lamellas of the cornea are without nuclei. The free space is an artefact, and the dark area is blood. The iris is totally necrotic, and to the right it appears as a mere shadow. The zonular fibers are dissolved, and the lens has fallen back.

the eye, a fibrinous, plastic exudate is thrown out by those preexisting tissues that survive, mostly from the sclera, and in time all dead parts are replaced by dense connective tissue. An ordinary cyclitic membrane is deliminated from the vascular layer of the ciliary body by the pigment epithelium. In necrosis the pigment epithelium is destroyed, so that the membrane, containing pigment granules, scattered freely or held in phagocytes, is matted with the remains of the ciliary body and iris. Rapid shrinkage of the eye ensues, far more rapid than ever occurs in ordinary iridocyclitis.

It is conceivable that every tumor cell is dead and that the shrunken globe represents a spontaneous regression of the disease. This may also happen in cases of retinoblastoma. With either neoplasm such an event must be extremely rare. Somewhere a few melanoma cells survive and multiply to fill the shrunken globe and to break out in time through the fibrous envelope and push the stump of a globe forward.

NECROSIS ARTIFICIALLY INDUCED

1. *As a Therapeutic Measure.*—It is interesting that two diseases of the eye, retinoblastoma and detachment of the retina, formerly considered

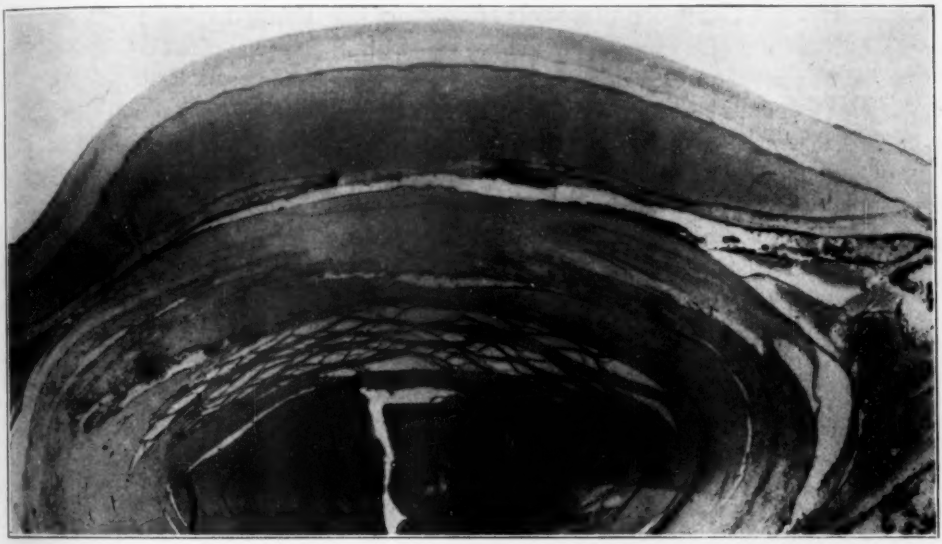

Fig. 10.—Necrosis of the iris superimposed on atrophy, caused by toxins from an almost completely necrotic malignant melanoma of the choroid. The corpuscles are absent in the posterior layers of the cornea. The pigment epithelium of the iris is detached on the right side. There is an anterior polar cataract.

hopeless, may now be cured by the induction of tissue death. It is one of the triumphs of irradiation that the rays can be so concentrated and directed as to destroy the neoplasm without damaging the normal structures of the eye. One theory is that the necrosis is brought about by the rays as the result of closure of the blood vessels, and not as the result of the direct action on the cells.

2. *As a Surgical Procedure.*—In diathermy for reattachment of the retina, each separate puncture through the sclera causes a break in continuity which has to be repaired. Bordering each hole in the sclera is a zone of total coagulation necrosis, cells and bundles of connective tissue all being killed. Surrounding this is another zone of incomplete coagula-

tion, in which the cells only are killed. The result is that from the two zones inflammatory toxins spread into the adjoining sclera and choroid and into the retina, once it is brought into opposition. Time must elapse before the inflammatory reaction can produce the cohesion of the retina, choroid and sclera. The greater the damage to the parts, the longer delayed and the severer the reaction. This may manifest itself clinically by the escape of red blood cells in the tissues or hemorrhage into the vitreous.

Each whitish spot that in time marks the site of a puncture represents much more than a similar-looking spot left after the healing of a focus of naturally produced chorioretinitis. The artificially produced spot is in reality the protrusion of a sheet of compact scar tissue that encompasses the sclera and is inseparably interwoven with it.

A wide expanse of the sclera is sometimes punctured in one or more operations, and often the coagulated areas infringe on one another, so that a large area of the fibrous tunic of the eyeball is made necrotic and must be replaced by tissue, baser than the original, which process requires an indefinitely long period. To gain more intense reaction within the eye, the surface of the sclera is cauterized until its bundles shrink and quiver. There is also the trauma involved in making a large exposure and in tenotomizing a muscle. In obliterating the perichoroidal lymph space, its lamellas and the nerves, arteries and muscle fibers that lie in the space are destroyed. The lymph space of Tenon is effaced. These artificially produced changes, summed up, must play a potent role in the causation of the uveitis and cataract that not infrequently develop a few months, or a few years, after diathermy, even when the retina is in place.

57 West Fifty-Seventh Street.

INCIDENCE OF DEFECTIVE COLOR VISION AMONG PSYCHOTIC PATIENTS

LeGRAND H. HARDY, M.D.

GERTRUDE RAND, Ph.D.
AND
M. CATHERINE RITTLER, A.B.
NEW YORK

INTEREST in the incidence of color blindness among psychotic patients has recently been aroused by the report in 1945 of Kaplan and Lynch [1] from the Hudson County Hospital of Mental Diseases, Secaucus, N. J. These authors concluded that psychotic patients, both male and female, show a high incidence of defective color vision. Of a group of 223 male schizophrenic patients, for example, they claimed to find evidence of defective color vision in 32.8 per cent, and of a group of 148 female schizophrenic patients, in 4.8 per cent. The generally accepted values for incidence of anomalies in color vision among male and female persons of the white race are, in round numbers, respectively, 8 and 0.5 per cent. The incidence claimed by Kaplan and Lynch is, then, approximately four times as great in male and nine to ten times as great in female psychotic subjects as that among subjects who are not mentally disoriented. The theoretic implications of this observation are of sufficient importance to warrant further investigation of the subject.

This is particularly evident since these results are at variance with the values reported in 1935 by Millard and Shakow [2] from the Worcester State Hospital, Worcester, Mass. These authors argued convincingly that it is necessary to use "stricter-than-the-usual criteria for diagnosing color-blindness" in a psychotic population, that evidence must be had that the responses given to the test for color blindness indicate a real defect in color vision, not merely agnosia-like symptoms, false perception or lack of concentration. Using such criteria, they concluded that the incidence of color blindness in a psychotic population,

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From the Knapp Memorial Laboratory, Institute of Ophthalmology, Columbia University College of Physicians and Surgeons.

1. Kaplan, H. M., and Lynch, R. J.: Color Blindness in the Psychoses, Am. J. Psychiat. **101**:675-676 (March) 1945.

2. Millard, M. S., and Shakow, D.: A Note on Color-Blindness in Some Psychotic Groups, J. Social Psychol. **6**:252-256 (May) 1935.

such as the one studied by them, in which 839 cooperative subjects were examined, including 329 male and 301 female schizophrenic patients, is not significantly different from that in the normal population.

In evaluating these two studies, several questions are raised which lead to opposite conclusions. These refer to the tests used to detect the presence of defective color vision, the criteria used in diagnosis and the administrative procedure.

REPORT OF MILLARD AND SHAKOW [2]

Millard and Shakow employed the Ishihara test.[3] This test had been used extensively by Miles, Garth and others in studying normal populations, and it was fairly well understood in 1935 what type of response could be expected from persons whose color vision is normal and what type from those whose color vision is defective. Miles's criterion [4] for diagnosing color blindness was widely adopted. He omitted from the test the 3 plates designed for illiterate subjects (the "path" plates), as well as plates 10 and 11, on which a digit is supposedly read only by those with defective color vision but actually is seen by many whose color vision is normal. When, then, 11 of the original 16 plates of the Ishihara test are used, Miles's criterion for anomaly in color vision is 2 or more plates incorrectly read. It should be noted that this criterion was based on the responses of 1,286 male university students, of whom 8.2 per cent had color vision diagnosed as defective. The diagnosis was based on the Ishihara test alone, without supporting evidence from other tests. Moreover, the group examined comprised a highly selected sample of the population as to age and intelligence. A strict application of Miles's criterion to all subjects is not, therefore, a priori valid.

It is known that insignificant errors in reading the plates may be due to factors other than defective color vision—for example, low visual acuity, inattentive observation of the plates and, in a psychotic population, false perception or report. To meet this difficulty, Millard and Shakow divided the responses to the plates of the Ishihara test into four groups: correct, color blind, anomalous (in which the correct or the "color-blind" figure was seen in part, or the response was apparently due to some bias of the subject) and doubtful (in which the response was anomalous but definitely suggested that the subject saw a figure which is considered to indicate a color-blind response). They experimented with several criteria, the most logical and successful of

3. A personal communication from Dr. Shakow indicates that the fifth edition of the Ishihara test was used.

4. Miles, W.: One Hundred Cases of Color-Blindness Detected with the Ishihara Test, J. Gen. Psychol. **2**:535-543 (Oct.) 1929.

which they called the Worcester III criterion. According to this, two or more definitely color-blind responses, excluding those to plates 10 and 11, were required as evidence of color blindness. On this basis, no color-blind female patient was found among the 301 examined, all of whom were schizophrenic; 8 per cent of the male psychotic patients (538) and 8 per cent of the male schizophrenic patients (328) were found to have defective color vision. By the Miles criterion, which Millard and Shakow felt to be inapplicable to the type of subjects they were examining, these percentages were 13 for the male aond 3 for the female schizophrenic group. Millard and Shakow stated that, in their opinion, the incidence of color blindness in Miles's population would not be materially changed by adoption of the Worcester III criterion and that it is valid to compare the percentage of color blindness found by Miles in a normal population with the percentage they found in a psychotic group.

REPORT OF KAPLAN AND LYNCH[1]

In this study, the American Optical Company's compilation of Pseudo-Isochromatic Plates was used. This test is a compilation of some Ishihara and some Stilling plates produced in 1940 to meet a government demand for a test for color blindness obtainable in this country in sufficient quantity to supply all military testing stations. An instruction booklet was furnished, which has since proved to be inadequate and misleading, and no critical scores were supplied to differentiate between normal and defective color vision performance. In 1942 Gallagher, Gallagher and Sloane[5] made a critical evaluation of the individual plates of this test, after having found that only a small percentage of 726 male adolescents gave the correct response to every plate, that a large number failed more than 10 per cent of the plates and that a variety of responses was made to the same plate by persons with apparently normal color vision. The result was that the diagnosis as to the color vision of many subjects was in doubt. This has been the general experience of others who have administered this series of plates in the military services, in industry and in schools. For example, in our examination of 365 subjects whose color vision by other tests was judged to be normal, 95 per cent failed to read all the plates correctly, 46 per cent failed 6 or more of the plates, and 14 per cent failed 10 or more.[6] Rarely was there complete failure to see a digit, such as

5. Gallagher, J. R.; Gallagher, C. D., and Sloane, A. E.: A Critical Evaluation of Pseudo-Isochromatic Plates and Suggestions for Testing Color Vision, Yale J. Biol. & Med. **15**:79-98 (Oct.) 1942.

6. Hardy, L. H.; Rand, G., and Rittler, M. C.: A Screening Test for Defective Red-Green Vision, J. Optic. Soc. America **36**:610-614 (Oct.) 1946; Arch. Ophth. **38**:442-449 (Oct.) 1947.

usually occurs when color vision is defective. Rather, the usual type of error was a misreading of digits because of careless observation, such as *48* for *43* (plate 2), a misreading of the Stilling digits of German formation, such as *25* for *75* (plate 30), the reading of the "invisible" digits (plates 33 and 34) or the combining of part of the correct and part of the "color-blind" response in the Ishihara type plates, such as *20* for *29* (plate 11). It is now generally recognized that this compilation of pseudoisochromatic plates has little diagnostic value, owing in large part to the inclusion of so many plates likely to be misread because of factors other than defective color vision.

This fault makes it impossible to establish an error score that will differentiate between normal and defective color vision performance. For example, some of our observers whose color vision was judged to be defective by other accepted criteria failed as few as 10 plates, whereas some whose color vision was similarly judged to be normal failed as many as 17 plates. There is, thus, a range in error score from 10 to 17 within which the diagnosis as to color vision is in doubt.

In the work of Kaplan and Lynch, no validation of the American Optical Company's compilation seems to have been made, or any administration of the test to a nonpsychotic population. They mentioned "the weakness of chart tests including their failure to test color perception" and pointed out that "some features are especially difficult for disoriented mental patients." They recognized also that the "tests do not determine the exact gravity of the color defect." Nevertheless, they classified their subjects into four categories without identifying the criteria on which these categories are based. They stated [1]:

> A small number of patients, practically all males, with an incomplete total color blindness, comprises the first group. They present a deficiency in the red-green sense together with a slight weakness in the blue-yellow sense. The greatest number of color defectives are in the second group. All of its members are simply red-green blind but they differ in grades of severity. The heading, color weakness, is descriptive of the third group. This category includes patients who have showed a genuine hesitancy or who have incorrectly read some few plates. . . . . Individuals without color defect are placed in the fourth group.

On the basis of these vague criteria, they concluded that "compared with known normal values, psychotic individuals show a high incidence of color defect" and that "psychotic females are afflicted with partial color blindness in comparatively high numbers." In view of what has already been said of the many random errors made by nonpsychotic subjects whose color vision is normal, the test records of Kaplan and Lynch need to be restudied before their conclusions can be accepted.

In final evaluation of the studies made by Millard and Shakow and by Kaplan and Lynch, it should be pointed out that the latter made no

mention of the conditions of illumination under which the color tests were made, and that the former used what they call "adequate daylight conditions." The variability in the color composition of daylight from dominant yellow to dominant blue and the need for standardization and control of this aspect of the illuminant used with pigment test material have been emphasized by one of us (L. H. H.) [7] and others since 1931, at which time standard illuminants for this type of work were adopted by the International Commission on Illumination (ICI).[8] Without this control test conditions are not constant; therefore, critical scores cannot be established between normal and defective color vision performance, and the results of color tests cannot be evaluated and interpreted correctly.

PRESENT INVESTIGATION

MATERIAL AND METHODS

This study was conducted at the New York State Psychiatric Institute. Dr. William A. Horwitz, associate clinical psychiatrist of the institute, arranged for the tests and supplied the medical diagnoses of the patients. When only those patients who were willing to take the tests and able to complete the series were included, there were 235 psychotic subjects, 123 male and 112 female. Of the male subjects, the diagnosis of schizophrenia was made for 106, of manic-depressive psychosis for 11 and of involutional psychosis for 2; 4 had miscellaneous psychoses. In addition, 37 male subjects with psychoneuroses were tested, chiefly patients with anxiety hysteria and obsessive-compulsive and reaction-compulsive neuroses. Of the female subjects, the diagnosis of schizophrenia had been made for 105, of involutional psychosis for 4, of manic-depressive psychosis for 2 and of Pick's disease for 1. In addition, 17 female patients with psychoneuroses were tested, chiefly patients with anxiety hysteria.

Conditions of Test Administration.—The tests were administered individually. The closest commercial approximation to ICI Illuminant C available at the present time was used to provide the illumination. (ICI Illuminant C approximates a color temperature of 6,750° K. and represents average overcast skylight.) This was obtained from the combination of a 100 watt, gas-filled tungsten lamp (color temperature 2,848° K.) and a Macbeth daylight glass filter, the combination giving a color temperature of 6,700° K. The level of illumination on the test material was above 25 foot candles, and the testing distance was about 30 inches (75 cm.).

Color Tests Employed.—Two tests were administered to all the subjects: (*a*) the Ishihara test (fifth edition),[9] utilizing, in addition to the demonstration plate, the 12 plates designed to detect defective color vision in literate subjects, and (*b*) the American Optical Company's compilation of Pseudo-Isochromatic Plates,[10] utilizing the 40 plates also designed to detect defective color vision in literate

7. Hardy, L. H.: Standard Illuminants in Relation to Color Testing Procedures, Arch. Ophth. **34**:278-282 (Oct.) 1945.

8. Smith, T., and Guild, J.: The C.I.E. Colorimetric Standards and Their Use, Tr. Optic. Soc. **33**:73-134, 1931-1932.

9. Ishihara, S.: Tests for Colour-Blindness, ed. 5, Tokyo, Kanehara, 1925.

10. Pseudo-Isochromatic Plates for Testing Color Perception, Philadelphia, Beck Engraving Co., 1940.

subjects. In addition, when the presence of defective color vision was found or suspected, recourse was had to the Hardy-Rand-Rittler Polychromatic Plates [11] for verification of the diagnosis.

Criteria Used to Diagnose Anomaly in Color Vision.—Ishihara Test for Color-Blindness: Following the criterion established by us [12] for this test administered under Macbeth daylight illumination, the misreading of 3 or fewer of the 12 plates utilized was taken to indicate normal color vision, and the misreading of 5 or more of the plates, to indicate defective color vision.

American Optical Company's Compilation: As has been stated, we were unable to establish a critical score that would screen normal from defective color vision when all 40 plates of this compilation were used. When, however, certain 22 of the plates were discarded as worse than useless, i. e., misleading, we were able to establish such a score, utilizing the remaining 18 plates.[6] With this 18 plate selection, the misreading of 4 or fewer plates indicates color vision within normal limits and the misreading of 5 or more plates indicates defective color vision, provided the test is administered under Macbeth daylight illumination. For each subject tested, however, the error score was computed (*a*) on the 40 plate series which was used by Kaplan and Lynch and (*b*) on our revised selection of 18 plates.

TABLE 1.—*Incidence of Defective Color Vision Among the Psychotic and Psychoneurotic Subjects Tested* *

Group	Sex	Number of Patients Examined	Defective Color Vision	
			Number	Per Cent
All psychoses	M	123	10	8.1
Schizophrenia	M	106	10	9.4
Other psychoses	M	17	0	0.0
Psychoneurosis	M	37	3	8.1
All psychoses	F	112	2	1.8
Schizophrenia	F	105	2	1.9
Other psychoses	F	7	0	0.0
Psychoneurosis	F	17	0	0.0

* Diagnosis as to defective color vision was based on the Hardy-Rand-Rittler criteria for the Ishihara test and the 18 plate selection from the American Optical Company's compilation and on the Hardy-Rand-Rittler Polychromatic Plates.

RESULTS

A general statement of the results obtained follows. Of the 123 male psychotic patients, 10 (8.1 per cent), and of the 112 female psychotic patients, 2 (1.8 per cent), had defective color vision. Of the 37 male psychoneurotic patients, 3 (8.1 per cent) had defective color vision, and in the 17 female psychoneurotic patients no case of anomaly in color vision was found. All the patients were consistently classified as to normal or defective color vision by our criterion for the Ishihara test and by our criterion for the 18 plate selection from the American Optical Company's compilation. The results are shown in table 1.

11. Hardy, L. H.; Rand, G., and Rittler, M. C.: Color Vision and Recent Developments in Color Vision Testing, Arch. Ophth. **35**:603-614 (June) 1946.

12. Hardy, L. H.; Rand, G., and Rittler, M. C.: Tests for Detection and Analysis of Color Blindness: I. An Evaluation of the Ishihara Test, Arch. Ophth. **34**:295-302 (Oct.) 1945.

As is seen in table 1, all the psychotic patients with the diagnosis of defective color vision belonged in the large group of schizophrenic patients. The incidence of defective color vision for the male schizophrenic subjects was 9.4 per cent, and that for the female schizophrenic subjects, 1.9 per cent. The question arises whether these figures furnish evidence of a higher incidence of defective color vision in the schizophrenic groups than would be found in normal groups of the same size.

Accepting 8 per cent as the incidence of defective color vision in the normal male population, we find from computation from the normal curve that the magnitude of the difference found by us (1.4 per cent) is such that it could have been equaled or exceeded 60 per cent of the time in chance samples of 106 subjects. For this reason, the incidence of 9.4 per cent found in our schizophrenic group has no statistical significance and would be expected from chance factors alone.

The incidence of defective color vision in the normal female population (0.5 per cent) lies in the realm of small samples—the Poisson realm. Calculation of the Poisson distribution shows that an incidence of anomaly in color vision of 1.9 per cent could be equaled or exceeded 10 per cent of the time by chance variation. There appears, then, to be no statistical significance in the incidence of defective color vision found in our female schizophrenic group.

From the results of our study we conclude, therefore, that in the general group of psychotic patients tested by us, as well as in the special group of schizophrenic patients, there is no significantly higher incidence of anomaly in color vision than would occur in nonpsychotic groups of the same size. This conclusion is in agreement with that of Millard and Shakow and in disagreement with that of Kaplan and Lynch.

In the attempt to see whether there are any differences of note between the responses to pseudoisochromatic tests made by nonpsychotic patients and the responses made by psychotic patients, and to offer an explanation, at least in part, of the conclusion reached by Kaplan and Lynch, an analysis was made of the number of errors and the individual plates failed by members of our psychotic group and by nonpsychotic subjects whom we had examined under the same conditions with the Ishihara test and with the American Optical Company's compilation of color plates.

Ishihara Test.—On this test we have for comparison the records of 71 nonpsychotic and 223 psychotic subjects whose color vision was judged normal. Table 2 shows the number of plates failed by the members of each sex in each group and by each group as a whole. It is seen in this table that the range of error scores is the same for the nonpsychotic and for the psychotic group and that the distribution of error scores is quite similar, with the exceptions that fewer of the psychotic patients made a perfect score and more failed one or two plates

(columns 4 and 7). A comparison of columns 2 and 5, which give the distribution of errors made by the male subjects of each group, and of columns 3 and 6, which give this distribution for the female subjects, shows that the greater number of errors made by the psychotic group as a whole was due almost entirely to the tendency of the psychotic female patients to make many more random errors than were made by the nonpsychotic female subjects. The distribution of errors for the male subjects of the two groups is very similar.

An analysis of the individual plates of the Ishihara test failed by the members of the two groups who had normal color vision showed that plates 5, 10 and 11 were most frequently failed. Plate 5 was misread by 27 per cent of the nonpsychotic and by 35 per cent of the psychotic group. Instead of *74,* the number was most often read as *71.* Other responses were *24, 91, 11* and *21.* The color-blind response *21* was given by 6 per cent of each group. It is our experience that this

TABLE 2.—*Results for Ishihara Test (Fifth Edition), Showing for Comparison Number of Plates Failed by 71 Nonpsychotic and 223 Psychotic Subjects All of Whom Were Judged to Have Normal Color Vision* *

Number of Plates Failed	Nonpsychotic Group			Psychotic Group		
	Males (33), per Cent	Females (38), per Cent	Total (71), per Cent	Males (113), per Cent	Females (110), per Cent	Total (223), per Cent
0	45.5	63.2	54.9	46.9	38.2	42.6
1	33.3	28.7	28.2	36.3	39.1	37.7
2	18.2	10.5	14.1	13.3	20.0	16.6
3	3.0	2.6	2.8	3.5	2.7	3.1

* The 12 plates designed to test color vision among literate subjects were used.

single color-blind response is not evidence of defective color vision provided it is the only typically color-blind response, excluding those to plates 10 and 11, on which plates some pattern was frequently seen by members of each group.

Finally, we have for comparison on the Ishihara test the records of 74 nonpsychotic and of 12 psychotic subjects whose color vision was judged to be defective. The range of error scores for the former group was 5 to 12 [13] and for the latter group 7 to 12.

13. It may be of interest to note that the criterion of Miles and the Worcester III criterion of Millard and Shakow were also applied to the test records of our psychotic and nonpsychotic subjects of both the groups with normal and the groups with defective color vision. The criterion of Millard and Shakow gave a diagnosis as to color vision that was consistent in every case with our own. On the Miles criterion, however, 4 additional members (6 per cent) of the nonpsychotic group, 3 male and 1 female subjects, and 6 additional members (3 per cent) of the psychotic group, 3 of each sex, would have been rated as having defective color vision.

American Optical Company's Compilation (40 Plates).—On this test, we have for comparison the records of 365 nonpsychotic and 223 psychotic subjects whose color vision was judged to be normal. Table 3 shows the number of plates failed by each sex of each group and by each group as a whole. As was the case in table 2, table 3 also shows that the range of error scores is the same for the nonpsychotic and for the psychotic group and that the distribution of error scores is, with minor exceptions, very similar (columns 4 and 7). For each group the maximum error score was 17, and the median error score, 5. A comparison of the distribution of errors for the two groups for each sex considered separately shows even more strikingly than in the Ishihara test that theh psychotic female subjects made many more random errors than the nonpsychotic female subjects.

TABLE 3.—*Results for American Optical Company's Compilation of Pseudo-Isochromatic Plates, Showing for Comparison Number of Plates Failed by 365 Nonpsychotic and 223 Psychotic Subjects All of Whom Were Judged to Have Normal Color Vision* *

Number of Plates Failed	Nonpsychotic Group			Psychotic Group		
	Males (222), per Cent	Females (143), per Cent	Total (365), per Cent	Males (113), per Cent	Females (110), per Cent	Total (223), per Cent
0 or 1	7.2	18.9	12.6	12.4	8.2	10.3
2 or 3	16.7	25.2	18.4	29.2	20.0	24.7
4 or 5	25.2	19.6	23.0	22.1	20.0	21.1
6 or 7	19.8	16.0	19.2	15.0	20.0	17.5
8 or 9	16.7	7.0	13.0	8.9	10.0	9.4
10 or 11	6.8	7.0	7.1	7.1	14.5	10.8
12 or 13	4.9	4.9	4.4	3.5	0.9	2.2
14 or 15	1.8	1.4	1.7	0.9	2.7	1.8
16 or 17	0.9	0.0	0.6	0.9	3.6	2.2

* The 40 plates designed to test color vision among literate subjects were used.

An analysis of the individual plates of this test failed by the members of each group who had normal color vision showed nothing of significance, with the possible exception that more of the psychotic group tended to see part of the "color-blind" number on Ishihara type plates 11 and 12 and more tended to see some pattern on the "invisible digit" plates 33 and 34. In general, however, the plates that were failed by a comparatively high percentage of the nonpsychotic group were failed also by a high percentage of the psychotic group, and those that were failed by a low percentage of the nonpsychotic group were similarly failed by a low percentage of the psychotic group.

A comparison of the number of plates failed by the 117 nonpsychotic subjects and the 12 psychotic subjects having defective color vision shows that the range of error scores for the former group was 10 to 38,[6] and that for the latter group, 10 to 39.

Chart 1 shows the distribution of the number of plates failed on the 40 plate compilation for both the subjects with normal and the subjects with defective color vision in the nonpsychotic and in the psychotic group tested by us. In this chart, rectangles in outline present the data for subjects whose color vision was judged to be normal; black rectangles, data for subjects whose color vision was judged to be defective. Data for the nonpsychotic group are given in the left hand rectangles, and data for the psychotic group, in the right hand rectangles. For readier identification, the rectangles which present the data for the psychotic group are striped diagonally, black on white indicating normal color vision and white on black indicating defective color vision. The number of plates failed (error score), in steps of 2, is

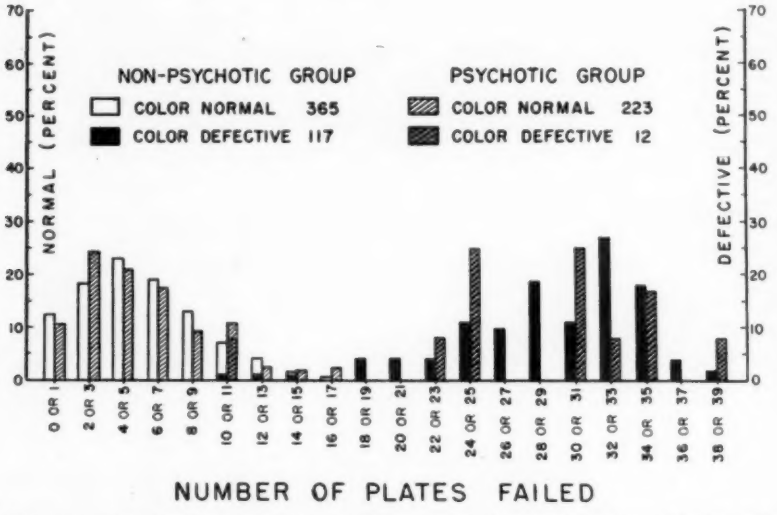

Fig. 1.—Distribution of number of plates failed in the American Optical Company's compilation of 40 Pseudo-Isochromatic Plates for subjects with normal and for subjects with defective color vision in both the nonpsychotic and the psychotic group.

plotted on the horizontal coordinate, and the percentage of cases, on the vertical coordinate. Chart 1 clearly shows the general similarity of the distributions of error scores for the two groups of subjects with normal color vision. It also shows for both groups the same overlapping range of 10 to 17 errors within which the diagnosis of normal or defective color vision is in doubt.

In concluding the discussion of this test, we wish to say that, in our opinion, the observation by Kaplan and Lynch of a high incidence of defective color vision among psychotic subjects was in major part due (*a*) to poor selection of the test for color blindness used in the study, (*b*) to ignorance of the many random errors which nonpsychotic sub-

jects whose color vision is normal make on this test and (*c*) to inadequate criteria on which to base the diagnosis of defective color vision. Lack of control of conditions under which the test was administered may also have been a contributing factor.

TABLE 4.—*Results for American Optical Company's Compilation (18 Selected Plates), Showing for Comparison Number of Plates Failed by 365 Nonpsychotic and 223 Psychotic Subjects All of Whom Were Judged to Have Normal Color Vision*

Number of Plates Failed	Nonpsychotic Group			Psychotic Group		
	Males (222), per Cent	Females (143), per Cent	Total (365), per Cent	Males (113), per Cent	Females (110), per Cent	Total (223), per Cent
0	66.1	81.2	72.0	65.5	67.3	66.4
1	25.3	15.3	21.4	24.8	20.0	22.4
2	4.1	2.8	3.6	8.0	6.5	7.2
3	3.2	0.7	2.2	1.7	5.4	4.6
4	1.3	0.0	0.8	0.0	0.9	0.4

TABLE 5.—*Results for American Optical Company's Compilation (18 Selected Plates), Showing for Comparison Percentage of Nonpsychotic and Psychotic Group Having Normal Color Vision Who Failed Each Plate of This Selected Series* *

Plate Number	Nonpsychotic Group			Psychotic Group		
	Males (222), per Cent	Females (143), per Cent	Total (365), per Cent	Males (113), per Cent	Females (110), per Cent	Total (223), per Cent
3	1.8	0.7	1.4	0.0	1.8	0.9
4	5.0	1.4	3.6	0.9	4.5	2.7
5	0.0	0.0	0.0	0.9	0.0	0.5
6	0.0	0.0	0.0	0.0	0.0	0.0
8	11.3	3.5	8.2	2.7	6.3	4.5
9	0.5	0.0	0.3	0.9	0.0	0.5
12	8.1	4.9	6.6	18.6	12.7	15.7
13	0.5	0.0	0.3	0.0	3.6	1.8
16	0.0	0.0	0.0	0.0	0.0	0.0
17	4.5	2.1	3.6	3.5	5.5	4.5
19	0.0	0.0	0.0	0.0	0.0	0.0
20	2.3	0.7	1.6	5.3	7.3	6.3
21	5.4	2.8	4.4	2.7	7.3	4.9
23	1.8	1.4	1.6	0.9	0.9	0.9
27	3.2	2.8	3.2	3.5	3.6	3.6
29	1.4	2.1	1.6	3.5	1.8	2.7
41	0.0	0.0	0.0	0.9	0.0	0.5
42	9.0	0.0	5.5	3.5	0.9	2.2

* Each plate is designated by the number of its occurrence in the full compilation.

American Optical Company's Compilation (18 Selected Plates).—On this test we, again, have for comparison the records of 365 nonpsychotic and 223 psychotic subjects whose color vision was judged to be normal. Table 4 shows the number of plates of this series failed

by each sex of each group and by each group as a whole. Once more, the same similarities are shown between the nonpsychotic and the psychotic group as were seen in tables 2 and 3, that is, (*a*) the same range of error scores, (*b*) the same median error scores and (*c*) the general similarity in distribution of errors, with the exception of the tendency of the psychotic group to make more errors. This tendency is much less pronounced in this selection of 18 significant plates than it was in the full 40 plate compilation, and once more we find it was mainly due to the greater number of errors made by the psychotic female subjects.

Table 5 shows the plates used in this selected series and the percentage of each sex of each group and that of each group as a whole who

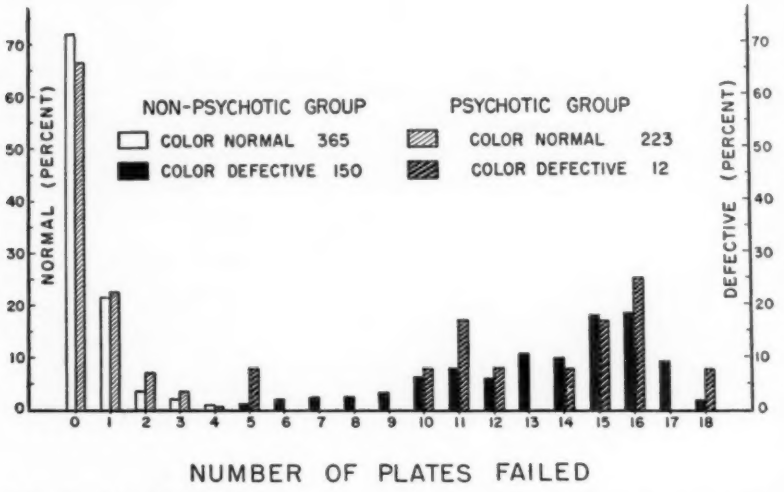
NORMAL (PERCENT)
DEFECTIVE (PERCENT)
NON-PSYCHOTIC GROUP
COLOR NORMAL 365
COLOR DEFECTIVE 150
PSYCHOTIC GROUP
COLOR NORMAL 223
COLOR DEFECTIVE 12
0 10 20 30 40 50 60 70
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
NUMBER OF PLATES FAILED

Fig. 2.—Distribution of error scores on the 18 plate selection of the American Optical Company's Pseudo-Isochromatic Plates for subjects with normal and for subjects with defective color vision in both the nonpsychotic and the psychotic group.

failed each plate. The plates are designated by the number of their occurrence in the American Optical Company's full compilation. The table shows little difference of significance between the responses of the groups compared, except for the responses to plate 12 already noted in the previous section and the higher percentage of errors made by the psychotic female subjects.

A comparison of the number of plates of this selected series which were failed by 150 nonpsychotic and the 12 psychotic subjects having defective color vision shows that the range of error scores for both the former and the latter group was 5 to 18.[6] It is thus seen that the critical score established for this series on a nonpsychotic group to

differentiate between normal and defective color vision performance holds for the psychotic group as well.

In chart 2 is shown the distribution of error scores on the 18 plate selection for both the subjects with normal color vision and the subjects with defective color vision in the nonpsychotic and psychotic groups. The data are presented in the same form as in chart 1. Chart 2 shows (*a*) the general similarity in the distribution of error scores for the two groups with normal color vision and (*b*) the same range of error scores for these groups when color vision is normal and when it is defective. In other words, in both groups with normal color vision no more than 4 plates were failed, and in both groups with defective color vision no fewer than 5 plates were failed.

CONCLUSIONS

The incidence of color blindness among the psychotic patients tested by us was not significantly higher than that among the normal population.

In our opinion, the contrary finding by Kaplan and Lynch was in major part due (*a*) to poor selection of the test for color blindness used in their study, (*b*) to ignorance of the many random errors made on this test by nonpsychotic subjects whose color vision is normal and (*c*) to inadequate criteria on which to base the diagnosis of the presence of defective color vision. Lack of control of conditions under which the test was administered may also have been a contributing factor.

23 East Seventy-Ninth Street.

PREPLACEMENT OF AIR IN CYCLODIALYSIS

SOL ROME, M.D.
AND
RAPHAEL KOFF, M.D.
LOS ANGELES

THE ADVANTAGES of the use of air after cyclodialysis have been fully discussed by Barkan [1] and several other writers in recent articles.[2] These advantages were summarized by Barkan as follows: The injection of air (1) controls hemorrhage, (2) widens the cyclodialysis cleft, (3) makes the cleft visible and (4) deepens the anterior chamber. He stated:

> Cyclodialysis combined with air injection is indicated in primary glaucoma of the wide angle type. It is especially indicated, to the exclusion of trephination, iridencleisis and iridectomy in the late stage of the narrow angle type after peripheral adhesions have closed the angle in large part, irrespective of whether there is congestion or not. It is indicated in those varieties of secondary glaucoma in which cyclodialysis is commonly accepted as being indicated, [e. g., aphakia]. . . . A high degree of pressure has not contraindicated its use.

In all the methods described in the literature the air is injected after the completion of the dialysis. For the past year we have routinely injected air into the anterior chamber as the first step in the operation, before the scleral incision for the cyclodialysis. This procedure was used originally in a case in which the anterior chamber was almost completely obliterated, in order to deepen the chamber. The lens-iris diaphragm was thus pushed backward, safely out of the way of the spatula.

Since then, cyclodialysis preceded by the injection of air has been performed on 9 eyes. The patients were private ones and were followed closely both before and after operation. In all cases the tension after operation was under 25 mm. (Schiøtz), continuously, although pilocarpine was required in 4 cases. The visual acuity and visual fields were maintained without loss in every case.

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1. Barkan, O.: Cyclodialysis, Multiple or Single with Air Injection: An Operative Technique for Chronic Glaucoma, California Med. **67**:78 (Aug.) 1947.

2. (*a*) Randolph, M. E.: A New Cyclodialysis Instrument, Am. J. Ophth. **26**:187 (Feb.) 1943. (*b*) Shaffer, R. N.: Inverse Cyclodialysis, ibid. **30**:860 (July) 1947. (*c*) Sugar, H. S.: Cyclodialysis: A Follow-Up Study, ibid. **30**:843 (July) 1947.

This modification of injecting air before the cyclodialysis incision, instead of after the operation, is an important one. It retains all the advantages of injecting air after operation. In addition, it prevents hemorrhage by avoiding sudden loss of intraocular pressure, since the preplaced air expands, replacing the volume of aqueous lost.

The hemorrhage most frequently occurs immediately on dialysis. A certain amount is already present before the spatula can be withdrawn and air injected. In other words, the postoperative injection of air arrests an already forming hemorrhage. Any blood present has a tendency to close the cleft, form synechias and thus nullify the operative result. Preoperative injection of air provides a cushion of air under slight pressure, which tends to prevent any bleeding at all, especially at the crucial moment of dialysis. The preoperative injection of air also deepens the anterior chamber and keeps it deep throughout the procedure. The iris is kept out of the way of the spatula by the air bubble. There are thus more room for the dialysis and less danger of injuring lens or iris and of peeling off Descemet's membrane, since the cornea does not have to be hugged as closely. As has been shown by Hughes and Cole,[3] air in the anterior chamber enables the angle of the chamber to be visualized without a contact lens. By preplacement of air, the angle and the cleft can be visualized during the entire procedure.

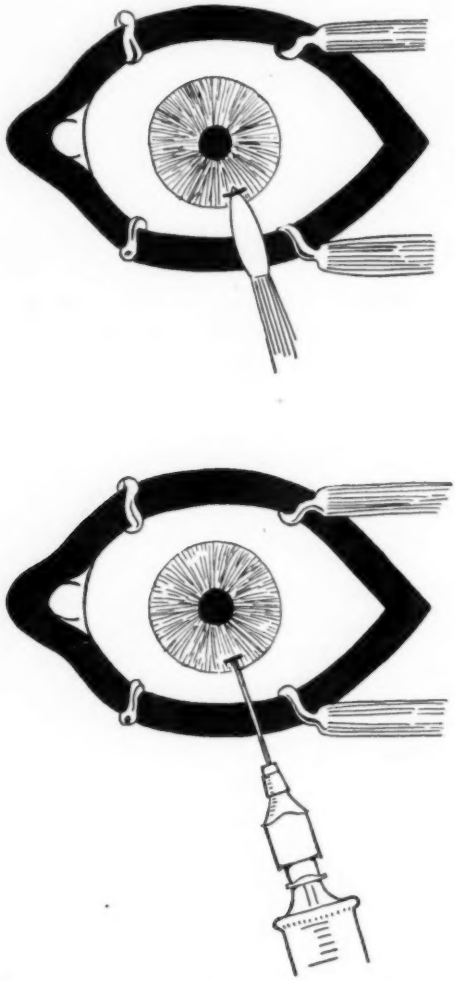
Technically, it is far easier to inject air into the anterior chamber before the operation, and there is far less risk. When the air is injected after operation, the eye is soft. The needle is inserted through a long tract, with only choroid separating it from the vitreous beneath. As Shaffer [2b] observed, there is always the possibility of puncturing the choroid or of the choroid herniating through the wound as the air pressure is increased.

PROCEDURE

The cornea is punctured at the limbus in the lower outer quadrant with either a Graefe knife or a small keratome. The point should pass just to Descemet's membrane, so that the aqueous does not escape. Air is drawn into a dry 2 cc. Luer syringe with a small hypodermic needle, 26 gage, attached. The needle is then inserted into the preformed opening, following the track of the previous incision. No aqueous is withdrawn. Approximately 1.5 cc. of air is injected into the anterior chamber. Enough is injected so that the iris is pushed back and the chamber is almost completely occupied by the air bubble. A narrow ring of aqueous usually remains at the limbus, sometimes in the form of small bubbles. The usual cyclodialysis is done in the upper outer quadrant, provided gonioscopic inspection shows no contraindication to this site. In sweeping the spatula, care must be taken not to pull up on the heel of the instrument. This

3. Hughes, W., and Cole, J.: Technical Uses of Air in Ophthalmology, Arch. Ophth. **35**:525 (March) 1946.

creates a vacuum along the tract, and the air in the anterior chamber is sucked out through the wound opening. The sweeping motion should be made with the tip of the spatula held against the sclera and the heel left in place as the fulcrum. There is a tendency, in trying to keep the tip of the spatula hugging the sclera, to pull up on the heel of the instrument. This should be avoided.



Upper figure, keratome incision at lower portion of limbus, just to Descemet's membrane; lower figure, insertion of needle through preformed track.

Immediately after withdrawal of the spatula the globe is compressed for a few minutes with two applicators, one at the scleral wound and one at the opposite portion of the limbus—at 8 o'clock if the incision is at 2 o'oclock.

Physostigmine is instilled after operation. The head of the bed is kept elevated continuously at an angle of 35 degrees, so that the air bubble rests against the cleft.

In all but 1 case, in which the air was lost through the cyclodialysis opening because of pulling up on the heel of the spatula, there was no, or almost imperceptible, bleeding, either immediate or late.

SUMMARY

Preplacement of air in cyclodialysis offers the following advantages over postplacement:

1. It is technically easier and safer.

2. It prevents hemorrhage, instead of arresting bleeding which has already commenced.

3. It facilitates the dialysis, especially in shallow chambers.

4. It allows visibility of the angle and of the cleft throughout the entire procedure.

5. There seem to be no contraindications.

1917 Wilshire Boulevard.

DEEP KERATITIS ASSOCIATED WITH ATYPICAL LICHEN PLANUS

Report of a Case

J. GOLDSMITH, M.D.
NEW YORK

RECENT studies [1] have shown that there is a close relation between prolonged quinacrine ("atabrine") medication and the development of cutaneous lesions bearing a striking resemblance to classic lichen planus. Because of this resemblance, the name "atypical lichen planus" was designated as the most appropriate term for the disease. It is my opinion that both the quinacrine medication and the subsequent cutaneous lesions played an important role in the production of the keratitis. This belief will be elaborated on later.

In all the literature dealing with this disease and in a personal observation of over 250 cases, only 1 case was encountered in which the deeper layers of the cornea were affected. This ocular involvement was particularly interesting not only because of its rarity but because of its close relation to the course of the cutaneous disease. It appeared during the height of the cutaneous disturbance and subsided in a manner closely paralleling the resolution of the dermatologic condition. The only other ocular lesions sometimes, though infrequently, seen in association with atypical lichen planus were blepharoconjunctivitis, conjunctivokeratitis and cutaneous lesions of the eyelids. Atypical lichen planus [2] is a new dermatologic entity, first seen during World War II. The cutaneous lesions have been classified as (1) atypical lichen planus, (2) atypical lichen planus with eczematoid characteristics and (3) eczematoid dermatitis. The first two types were observed only after prolonged ingestion of quinacrine. The third type seemed to be an acute allergic response to a single dose of quinacrine and

From the Department of Ophthalmology, Mount Sinai Hospital.

Read at a meeting of the New York Society for Clinical Ophthalmology, New York, Feb. 3, 1947.

1. Bazemore, J. M.; Johnson, H. H.; Swanson, E. R., and Hayman, J.: Relation of Quinacrine Hydrochloride to Lichenoid Dermatitis (Atypical Lichen Planus), Arch. Dermat. & Syph. **54**:308-324 (Sept.) 1946.

2. Rosenthal, J.: Atypical Lichen Planus (Southwest Pacific), Am. J. Path. **22**:473-491 (May) 1946. Dantzig, L., and Marshall, L. E.: Tropical Lichen Planus (New Guinea Variety): Clinical Report on Twenty-Four Cases (Possible Role of Quinacrine), New York State J. Med. **46**:991-995 (May 1) 1946.

occurred after an interval of several minutes to one week. More than one-half the patients showed two of the three types coexisting. In the Southwest Pacific area this disease became the most frequent cause of evacuation of patients with disabling cutaneous diseases.

REPORT OF CASE

History.—M. J., a white man aged 34, sergeant in the Army of the United States, had been in India since October 1944, after eight months' duty in New Guinea. Having received 55 Gm. of quinacrine hydrochloride U.S.P. as suppressive therapy since January 1944, he presented dryness and cracking of the skin involving the palms and fingers of both hands in May 1945, sixteen months later. The lesions extended along both forearms. The involvement of the skin was characterized by a purplish discoloration and a mild degree of itching. Shortly afterward, both legs and the external ears became involved in a similar manner. These lesions soon began to manifest a tendency to weep. He was hospitalized on July 3, 1945 at the 198th General Hospital and complained of blurred vision for the first time on Sept. 1, 1945, four months after the onset of the cutaneous disease. After continuous hospitalization for a number of weeks, with no definite response to therapy, he was returned to the United States and was transferred to the Battey General Hospital, arriving there on Sept. 30, 1945. The family and past histories were noncontributory. He denied having had venereal disease.

Physical Examination.—The normal weight was 180 pounds (81.8 Kg.); the present weight, 154 pounds (70 Kg.). The femoral, posterior cervical and auricular lymph nodes were enlarged. The oral mucosa was clear. The heart and lungs were normal. The blood pressure was 130 systolic and 74 diastolic. A roentgenographic study of the chest, examinations of the stool, blood count, urinalyses, serologic tests, malarial smears and hepatic function tests all gave results within normal limits. The skin in general was ichthyotic. There was a moth-eaten type of alopecia with multiple coin-sized, lavender, scaly patches on the scalp and similar-sized erythematous, atrophic areas. The pinnas and the external auditory canals were involved in an eczematoid process, with fissuring, and were swollen from a secondary infection. The ear drum membranes were intact. There was some scaling on the face, and the upper eyelids showed small, superficial patches of lavender, scaling dermatitis. Larger patches of the same type were present on the neck, in the axilla and in the crotch, but these areas were secondarily eczematized. Extending from above both knees, a diffuse eczematoid, weeping process spread along the dorsal aspect of the feet to the toes. The hands, dry and scaling, had a peculiar violaceous hue.

Ophthalmologic Study.—Vision was 20/70 in the right eye and could not be improved with a + 0.50 D. sphere, and was 20/20 in the left eye. Associated movements were full in all the cardinal directions. No muscular imbalance was noted. The right pupil was round and regular and reacted sluggishly to light and fairly well in accommodation; the left pupil responded normally. Intraocular tension appeared to be within normal limits on digital palpation. A slight circumcorneal flush was present in the right eye. Conjunctival lesions were searched for, but none was found. A faint, circular, diffuse haze with irregular margins, measuring approximately 5 mm. in diameter, was observed by sclerotic scatter within the pupillary area of the cornea (fig. 1). On examination with direct illumination, moderate swelling of the cornea centrally could be seen. This manifested itself by a bulging of the posterior part of the optic section toward the anterior chamber. Optic dissection of the tissues corresponding to this region

of the cornea, from anterior to posterior, revealed the following condition: The epithelial surface was smooth and clear. Bowman's membrane and the anterior half of the substantia propria appeared within normal limits. Several tissue clefts of varying sizes were present in the swollen posterior layers, which showed a moderate increase in relucence and many small, discrete, faint gray spots. Despite these, a number of folds in Descemet's membrane and a cluster of needle-shaped crystals plastered on the endothelium could be observed without difficulty. A polychromatic luster was reflected from the crystals when the beam from the slit lamp was shifted from side to side. A large number of precipitates, varying in

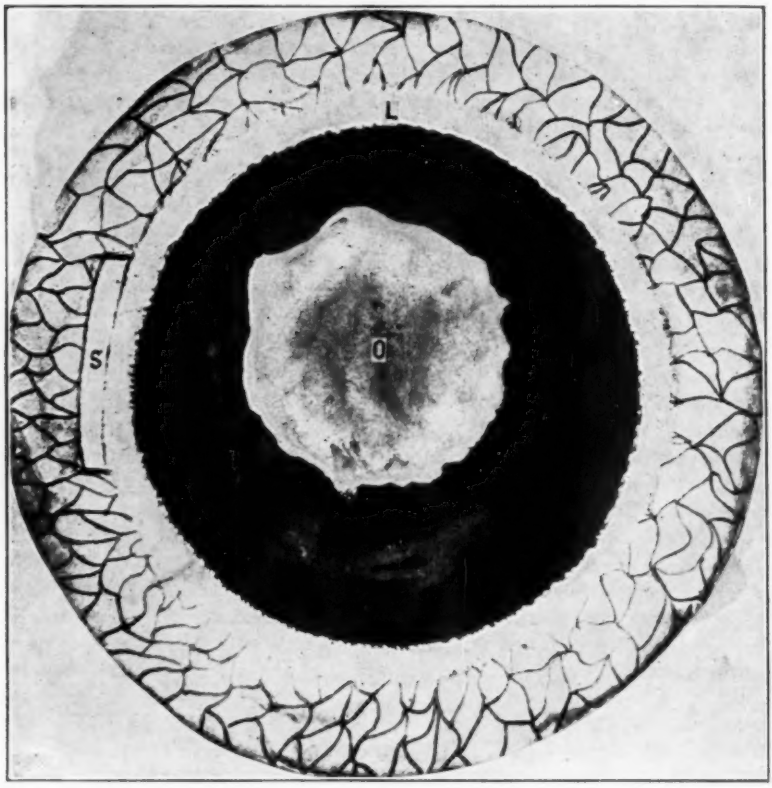


Fig. 1.—Sclerotic scatter, demonstrating (*O*) large central opacity of the right cornea, (*S*) beam of the slit lamp and (*L*) limbal glow.

size and shape, were strewn on and about the crystals. These deposits varied from gray to light brown. They decreased in number peripherally. The circular border of the interstitial infiltration extended to a zone about 3 mm. from the limbus, leaving a clear, circular band of cornea. In the right eye on upward gaze, a 2 plus aqueous flare was observed through the clear cornea. No posterior synechias were seen. The fundus could not be visualized through the undilated pupil. After its dilation, a sprinkling of fine cells was visible on the anterior capsule of the lens. No lenticular changes were noted. The fundus and vitreous appeared within normal limits. The left eye revealed no pathologic changes.

Diagnosis.—The diagnosis was (1) atypical lichen planus, with severe eczematoid characteristics; (2) keratitis of the right eye, acute, moderate, deep and probably secondary to the cutaneous disease, and (3) iritis of the right eye, moderate, low grade and secondary to the keratitis.

Subsequent Course.—On October 6, three months after his admission, reexamination revealed a slight increase in activity in the right eye. The cornea appeared more edematous, and there was an increased deposition of cellular elements on the endothelium. The substantia propria in proximity to Bowman's membrane showed an early increase in relucence. Twelve days later it was observed that the

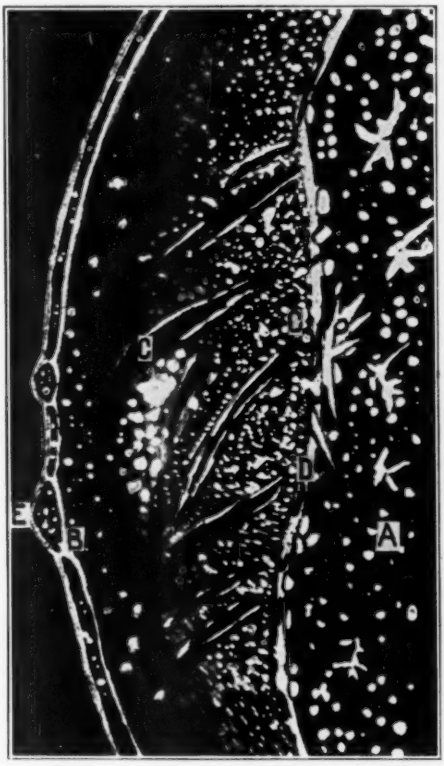


Fig. 2.—Optic section of figure 1, active stage. *E* indicates epithelial vesicle; *B*, folds in Bowman's membrane; *C*, tissue clefts, increased relucence and bulging of the posterior layers of the cornea; *D*, folds in Descemet's membrane and keratic precipitates and crystals on the endothelium; *A*, cells and fibrinous exudate in the anterior chamber.

corneal opacity had extended peripherally, approximately 1 to 2 mm. The bulbar injection had become more intense. Up to that time, the pathologic process had been localized principally to the posterior layers of the cornea. On this examination, however, it was found that the epithelial surface overlying the deep infiltration presented a number of small vesicles, varying in size from 1 to 2 mm. in diameter (fig. 2). Two of these vesicles appeared to have been broken recently, since one could easily discern their ragged and filamentous edges after they had been

stained with a 2 per cent solution of fluorescein sodium U.S.P. Bowman's membrane and the anterior third of the cornea showed a moderate increase in the number and degree of relucent areas, and several tissue clefts were present. The parenchymatous infiltration had become so pronounced that the details in the posterior layers could be demonstrated only with great difficulty. The aqueous flare was 4 plus, and the details of the fundus were obscured. Neither anterior nor posterior synechias could be found. Digital palpation of the right eye at this time gave no evidence of increased intraocular tension. The patient complained only of a persistent, dull, aching pain in the right eye.

Most of the cutaneous lesions slowly regressed under treatment, but several areas remained active and became excoriated, especially at night and in the morning. This excoriation was attended with increased weeping of the lesions. Roentgen treatment was ordered on October 27, to control the pruritis of the lower extremities. Additional local treatment consisted in use of cool compresses to the legs, alternating with the application of soothing ointments. This therapy was intended to combat the eczematoid component. Further improvement of the skin followed three intravenous injections of typhoid vaccine, beginning on Oct. 26, 1945, together with a decreased activity of the corneal infiltration. At this point, the dermatologist advised the transfer of the patient to a skin center, in view of the necessity for the continued treatment of both the skin and the eye.

Accordingly, on November 8, the patient was admitted to Moore General Hospital. The diagnosis of atypical lichen planus with eczematoid characteristics was confirmed by Lieut. Col. James M. Bazemore, chief of the skin center. It was further noted that the mucous membrane of the mouth was the site of lacelike lesions, typical of the disease. Further examination of the right eye disclosed the following picture: Vision was 20/50, uncorrectible. The eye showed slight ciliary injection with conspicuous bedewing of the epithelium immediately anterior to the circumscribed area of infiltration in the posterior layers of the stroma. Numerous folds were present in Descemet's membrane. A striking increase of keratic precipitates was noted. The pupil was well dilated and free of posterior synechias. The anterior capsule of the lens was strewn with fine white dots and with spots of brown pigment. The lens and vitreous were within normal limits. The left eye was normal.

The patient was given four more intravenous injections of typhoid vaccine, beginning November 15. The corneal bedewing and the circumcorneal flush were gone by November 30. The increased relucence of the posterior layers began to lessen, the folds of Descemet's membrane to flatten and the precipitates to clear to such a degree that the details of the iris could be made out more clearly. The edema of the center of the cornea became absorbed to such an extent that the cornea resumed almost its natural thickness.

The patient was given urologic clearance on November 23. Examination of the feces disclosed no ova or parasites. The serologic reactions were negative on November 29. Study of the blood demonstrated 5,050,000 red cells, 100 per cent hemoglobin and 5,600 white cells, with 56 neutrophils, 35 lymphocytes, 4 monocytes, 4 eosinophils and 1 basophil. Intracutaneous tests with purified protein derivative of tuberculin U. S. P. gave negative reactions in two dilutions. A roentgenogram of the paranasal sinuses revealed no abnormalities.

Since the condition of the right eye and that of the skin had shown such great improvement, the patient was granted a sixty day convalescent furlough. He returned to the hospital on Feb. 24, 1946, in excellent condition and spirits. The hair of the scalp had grown in almost completely except for some irregularity of the hair line over the temples and on the back of the head. A number of discrete, poliotic patches were present throughout the scalp, in proximity to small, round

or oval, slightly raised, purplish plaques, which showed evidence of scaling. The returning hairs were strong and not easily removed from the dry scalp. The skin of the upper portion of the forearms and the lower parts of the legs revealed the regressive changes characteristic of subsiding atypical lichen planus. These changes consisted of discrete, purplish macules of varying sizes and shapes, hyperpigmentation, vitiligo and slight atrophy of the skin.

At this time, examination of the right eye gave interesting results. Vision was 20/15 in the right eye and 20/20 in the left eye. There was no bulbar injection The epithelial surface was smooth and clear. The swelling of the central

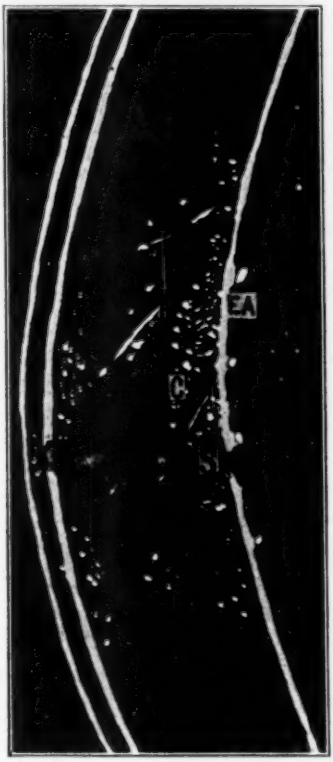


Fig. 3.—Optic section, healed stage. *S* indicates Stähli-Hudson line; *C*, several tissue clefts and faint relucence; *EA*, cells and keratic precipitates, which were occasionally seen.

parenchyma of the cornea had receded (fig. 3). Sclerotic scatter demonstrated the complete disappearance of the circumscribed corneal infiltration. A thin, horizontal Stähli-Hudson line, measuring 5 mm. in length, was seen 4 mm. above the lower limbus. Several tissue clefts were still found, but the relucent areas in the anterior, and especially in the posterior, layers of the cornea had faded out almost completely. No folds in Descemet's membrane could be discerned. A small number of fine precipitates, the majority of them colorless, still remained on the endothelial surface. An occasional cell floated in the anterior chamber. The iris, in middilatation, showed no posterior synechias. The fine deposits

on the anterior capsule of the lens had cleared up, so that it was now possible to see three congenital V-shaped pigment spots. The lens and the vitreous were clear. The fundus was normal.

It was apparent that the administration of penicillin, both intramuscularly and locally, to the eye in the form of drops and ointment had in no way altered the course of the keratitis, and that the direct application of sulfadiazine powder to the cornea had likewise proved ineffective.

Since the eye had recovered so satisfactorily, it was decided that the patient could be discharged on the basis of the condition of his skin. On March 8, 1946 he received a certificate of disability discharge and was instructed to present himself to the outpatient department of a veterans facility for further observation.

COMMENT

The atypical lichen planus observed during World War II resembled in the basic morphologic changes the classic lichen planus but, in addition, presented many unusual features. Poliosis, hyperpigmentation, vitiligo and alopecia, of various degrees and in all combinations, were frequently seen. The occurrence of aplastic anemia was also noted in some cases.

The keratitis associated with the present case was most interesting because of its unusual clinical course and its relation to keratitis profunda and keratitis disciformis. In another case of atypical lichen planus with aplastic anemia, a superficial punctate keratitis was demonstrated bilaterally.

The keratitis described in this paper closely simulated keratitis profunda, with two exceptions: (1) The anterior layers of the cornea were not involved in the earlier stages, and (2) no vascularization, deep or superficial, was ever present during any stage of the ocular involvement. Occasionally, a permanent deep opacity of the cornea persists in keratitis profunda, but this sequela did not develop in the present case.

Keratitis disciformis, which the keratitis here described also resembled, begins with localized central epithelial edema of the cornea, which eventually extends to the deeper layers. This process produces a central, indolent parenchymatous infiltration, characterized by a discoid form,[3] which then becomes permanent. In the present case, the pathologic process began in the posterior layers of the cornea centrally and spread anteriorly, and was followed by formation of vesicles in the epithelium in an area corresponding to the deeper infiltration. The cornea finally cleared, leaving a faint Stähli-Hudson line.

The pathologic alterations observed in this case did not conform to the classic clinical course and diagnostic morphologic changes which characterize the interstitial keratitides seen with syphilis and tubercu-

3. Berliner, M. L.: Biomicroscopy of the Eye, New York, Paul B. Hoeber, Inc., 1943, vol. 1, p. 519.

losis. In addition, the patient's reactions to serologic tests and to intracutaneous injections of tuberculin were negative on several occasions. That the keratitic process kept pace with the activity of the cutaneous lesions was clearly illustrated during several remissions and relapses. This parallelism strongly suggested a relationhip of cause and effect between the keratitis and the atypical lichen planus.

That certain types of infectious diseases of the skin may produce secondary inflammations of individual structures within the human eyeball has been recognized from time to time in previous publications. Participation in the disease process of the uveal tract, in part or as a whole, has been frequently described in cases of erysipelas, carbuncle, pemphigus, epidermolysis bullosa, urticaria, erythema nodosum, erythema exudativum multiforme and lichen planus.

Many cases of conjunctival involvement have been recorded with such conditions as molluscum contagiosum, Boeck's sarcoid, psoriasis, erythema nodosum, summer prurigo and acanthosis nigricans. The dermatogenous cataract has been seen as a complication following neurodermatitis, scleroderma, poikiloderma atrophicans vasculare, chronic eczema and Darier's disease (keratosis follicularis).

Keratitis not frequently has been associated with the following dermatologic conditions: acne rosacea, psoriasis, erythema exudativum multiforme, dermatitis herpetiformis, epidermolysis bullosa, xeroderma pigmentosum and pityriasis rubra pilaris.

The cause of atypical lichen planus remains unknown, but two lines of reasoning are worthy of consideration. 1. All the patients had received suppressive doses of quinacrine for long periods before the cutaneous eruption manifested itself. Discontinuance of the drug invariably resulted in decided improvement of the cutaneous lesions. Evidence has thus accumulated which supports the contention that quinacrine, acting as a toxic agent, could be responsible for the picture of atypical lichen planus. 2. All the patients with this type of eruption had been in the Southwest Pacific, particularly in New Guinea and on adjacent islands. It was noted that the cutaneous lesions began to regress in almost all patients who were removed from these regions. Of equal importance, therefore, is the possibility that climatic variations, pollens, various insects or irritants might have been responsible, as in contact dermatitis.

The first line of reasoning suggests a mechanism to explain the keratitis in the case reported here. I have observed that quinacrine is excreted perilimbally, its presence being demonstrated by sclerotic scatter as a yellowish green limbal glow. Epithelial edema[4] and super-

4. Chamberlain, W. P., Jr., and Boles, D. J.: Edema of Cornea Precipitated by Quinacrine, Arch. Ophth. **35**:120-134 (Feb.) 1946.

ficial pigmentation of the cornea and bulbar conjunctiva [5] have been noted in other cases after long-continued administration of the dye. Since the ciliary processes secrete the dye into the anterior chamber, the cornea is constantly bathed with a solution of quinacrine. This probably sensitizes the corneal tissues and renders them more vulnerable to other toxic substances. Since the keratitis in this case made its first appearance at the height of the cutaneous disorder (four months after the first cutaneous lesion appeared), and since it was not present during the preeruptive stage, it is logical to assume that toxic products formed by the destructive cutaneous lesions settled in the quinacrine-sensitized cornea, causing the keratitis described in this case.

SUMMARY

1. A rare case of deep keratitis occurring in atypical lichen planus associated with alopecia areata, poliosis, vitiligo and hyperpigmentation is described.

2. It is noted that vascularization of the cornea was not observed in this keratitic lesion, which finally underwent complete regression.

3. It is further noted that penicillin and sulfadiazine in no way altered the course of the keratitis.

4. The relation of this keratitis to keratitis profunda, keratitis disciformis and parenchymatous keratitis of the syphilitic and tuberculous types are discussed.

5. Atypical lichen planus is defined, and its three types are briefly outlined.

6. It is reasoned that quinacrine ("atabrine"), in the role of a sensitizing agent to the corneal tissues, was probably responsible for the development of the keratitis, together with toxic products of the destructive cutaneous lesions.

30 East Sixtieth Street.

5. Sugar, H. S., and Waddell, W. W.: Ochronosis-Like Pigmentation Associated with Use of Atabrine (Quinacrine), Illinois M. J. **89**:234-239 (May) 1946.

AN AID IN DETECTING TRACHOMA-LIKE INCLUSION BODIES IN THE CONJUNCTIVA

MARTIN BODIAN, M.D.
BROOKLYN

IN 1907, while in Java to investigate the immunology of syphilis, Halberstädter and von Prowazek [1] discovered the inclusion bodies associated with trachoma. This observation was the first demonstration of such bodies in the eye.

A few investigators have expressed the belief that the infectious agent of trachoma is a rickettsial body.[2] In support of this view, Cuénod and Nataf [2b] claimed the passage of the agent through the louse onto a normal conjunctiva, with the production of clinical trachoma.

Halberstädter-Prowazek inclusion bodies are observed in the conjunctival scrapings in cases of certain ocular infections. Although trachoma is the most important of these, similar bodies are also seen in cases of inclusion conjunctivitis, psittacosis and lymphogranuloma venereum.[3] Whether, as Lindner [4] stated, these bodies constitute the agent causing trachoma or whether they are the by-products of a tissue reaction to this agent is not clear. What does seem to be well established is that the bodies are to be found in the early phases of the infections noted. This fact is of great importance for the early diagnosis of these conditions. Since early diagnosis offers the best prospects of satisfactory therapy, the early detection of these inclusion bodies becomes proportionately important. The purpose of this paper is to indicate a method that will aid in the laboratory diagnosis of Halberstädter-Prowazek inclusion bodies in the conjunctiva.

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1. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1940, vol. 2, p. 1599.

2. (*a*) Busacca, A.: Is Trachoma a Rickettsial Disease? Arch. Ophth. **17**: 117 (Jan.) 1937. (*b*) Cuénod, A., and Nataf, R.: Researches on the Aetiology of Trachoma, Brit. J. Ophth. **21**:309, 1937; (*c*) Deuxième note sur la présence d'éléments infra-microbiens dans la follicules trachomateux, Arch. d'opht. **52**:573, 1935; (*d*) Sur la présence d'éléments rickettsoïdes très abondants et très constants dans les follicules trachomateux, Rev. internat. du trachome **12**:110, 1935.

3. Thygeson, P.: Viruses and Virus Diseases of Eye, Arch. Ophth. **29**:635 (April) 1943.

4. Lindner, K., in Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, p. 439.

PRESENT INVESTIGATION

While I was stationed with the Army in the Fiji Islands, a survey on trachoma among the inhabitants was conducted. In compiling the results of that study,[5] I needed photomicrographs to show the conjunctival inclusion bodies of trachoma. Many photographic technics were attempted in order to find the best means of demonstrating the inclusion bodies in stained conjunctival smears. With the use of different types of photographic color filters, various optical effects were produced. By this means was discovered a most satisfactory aid in detecting trachoma-like inclusion bodies.

Material.—All the smears which were positive for inclusion bodies were obtained from permanent inhabitants of the Fiji Islands. This population included Melanesians, Melanesian-Caucasian hybrids and East Indians.

The smears were obtained by scraping the upper tarsal conjunctiva with a semisharp instrument. This material was spread thinly on a glass slide, allowed to air dry and fixed with methyl alcohol for five minutes. Dilute Giemsa stain (1:10) adjusted to a p_H of 7.2 was then applied for twenty-four hours. After being washed with distilled water and dried with blotting paper, the slides were ready for microscopic study.

By oil immersion microscopy with white light the conjunctival epithelial cells were usually clearly demarcated. The cytoplasm took a pale blue stain, while the nuclei showed as a deep reddish violet. When inclusions were present, they could be seen as deep blue particles in any of their various phases of development. These bodies were most frequently observed in the cytoplasm in close propinquity to the nucleus. Many were seen as the characteristic "cape" formations described by Lindner[4] and others. When the microscopic picture was that just described, namely, a pale blue cell with a reddish violet nucleus containing characteristic formations of deep blue inclusions, diagnosis was indeed a simple matter. A single glance at the microscopic field gave the answer (figure).

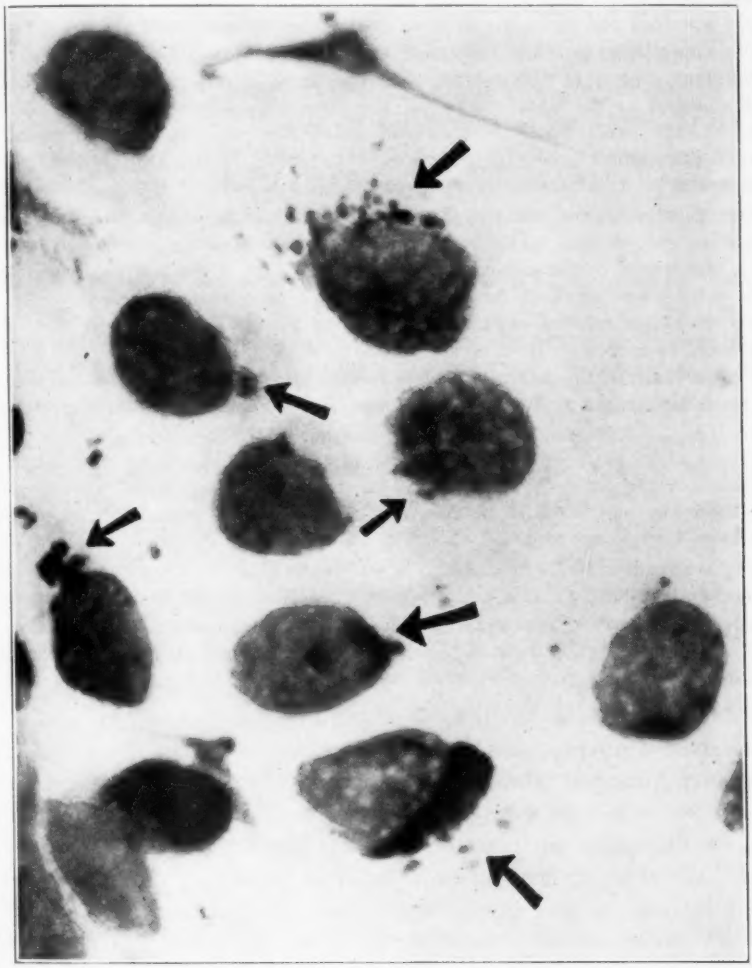
However, this happy mosaic did not always obtain. Occasionally the cytoplasm took on a dark reddish violet hue, which tended to obscure any inclusions present. This could not be accounted for on the basis of a faulty staining technic. Other slides subjected to the same conditions stained with perfect differentiation.

A second condition which on occasion hid the inclusion bodies was a jamming together of cells due to insufficient spreading during the making of the smear. As a result, nuclei overlay the cytoplasm of their neighboring cells. Inclusions that might be present in the cytoplasm were also covered by these nuclei. As has been noted, the reticulum of the nuclei characteristically stained a deep reddish violet. Because of its irregular meshwork and deep color, the nucleus frequently served as an excellent camouflage for any overlying or underlying inclusion bodies. Whenever possible, repeat smears were made in such instances. However, it was not always feasible to get our subjects back from their bush dwellings for this purpose. Clinic patients are often not more retrievable.

A third way in which inclusion bodies were occasionally obscured was by their occurring entirely within the nuclear contour. Fine focusing with the microscope

5. Bodian, M.: Trachoma: A Possible Carrier State, Arch. Ophth. **38**:450 (Oct.) 1947.

indicated that some were within the substance of the nucleus. Others, however, seemed merely in apposition with it—either above or below. As already noted, the nucleus, with its characteristic form and color, as brought out with the Giemsa stain, is an effective camouflage for Halberstädter-Prowazek inclusions. Unless one is prepared to spend a good deal of time on each field, employing the fine adjustment, one may easily overlook an inclusion lying within a nuclear border.



Photomicrograph (1,500 magnification) of conjunctival scrapings, showing Halberstädter-Prowazek inclusion bodies in epithelial cells Various phases and locations of the inclusion bodies may be noted (arrows). The photograph fails to show the cytoplasm of cells, but this can easily be seen in stained smears.

The aforementioned obstacles in the way of detecting inclusion bodies occurred often enough to be of significance. They were of particular hindrance during the course of a statistical survey in which hundreds of slides had to be studied. A single inclusion might be the only specific indicator on the entire slide. If this was missed, a false negative result would obtain. Those bodies which were

obscured by the means previously mentioned were particularly apt to be overlooked by ordinary microscopy.

Method.—By trial and error, it was found that the E, light red photographic filter (Wratten), series 23A, was the best in bringing out the inclusion bodies when stained by the Giemsa method. This filter transmits the longer wavelengths of light and absorbs the shorter ones. Thus, the red end of the spectrum passes through with little impediment. The blues and greens, however, are almost completely absorbed and hence are seen as shades of gray and black.

No appreciable variation in optical effect was discerned by placing the filter at different aspects of the microscope. The same effect was observed whether it was placed at the light source, on the substage condenser or in the ocular. Likewise, the exact material constituting the filter was relatively unimportant. Colored glass, sheet gelatin or plastic gave the same results, providing the wavelengths and color saturations were approximately the same.

One disadvantage of the red filter is that it tends to blur outlines of objects. This effect is produced by the wavelengths at the ends of the spectrum (red and blue), which tend to diminish visual acuity.[6] This loss of sharpness is so slight as to be of no consequence in the usual microscopic procedure. When, however, an infrequent object merited more exact study, the filter was removed so that white light could be used.

For general use, the gelatin filter was found most satisfactory. It is inexpensive, can easily be cut into desired sizes and shapes and is available in most photographic shops.

It was found more cumbersome to remove and replace filters from the substage condenser or the oculars. Hence, although the same optical effects were obtained from these locations, the most practicable method was used, namely, filtration of the light as it left its source.

In consideration of the discussion, it was found that the most convenient form of filter was a 3 inch (7.5 cm.) square of gelatin of the proper wavelength, mounted on a cardboard frame. This was placed before the substage microscopic lamp. When white light was desired for more minute structural delineation, the filter was simply removed. When the survey was resumed, the filter was as easily replaced.

Results.—For purposes of detecting inclusion bodies in the Giemsa-stained conjunctival smear, three structures are of particular importance: the pale blue cytoplasm of the conjunctival epithelial cell, its deep reddish violet nucleus and, not least, the deep blue inclusion body itself. When seen through the color filter previously noted, the cytoplasm becomes a pale gray, the nucleus is a medium gray and the inclusion bodies are an intense black, which stand out boldly from the surrounding field. Of course, the background is a uniform red.

Whatever structures have a red component in their stain are rendered less prominent by blending with the red background. This is especially important in the case of the nuclei, since these have a deep reddish element with the Giemsa stain, which effectively camouflages superimposed inclusion bodies in white light. With the red filter the

6. Duke-Elder,[1] 1939, vol. 1, p. 938.

nuclei are seen as a medium gray reticulum. Inclusion bodies within their contours stand out sharply in black relief. A passing glance shows their presence.

When the cytoplasm occasionally stains reddish, it acts much like the nucleus in hiding inclusion bodies. The red filter uncovers them from such situations, just as in the cases of nuclear superimposition.

COMMENT AND CONCLUSIONS

Several months after the technics described for studying inclusion bodies had been in use I came on a similar work by Caries.[7] He had used almost the same filter technic to facilitate the discovery of merozoites in blood smears of malarial patients. The blue-staining ring bodies in the red blood corpuscles stood out prominently with a red light filter. Apparently, he had no occasion to search for inclusion bodies. He found the method extremely helpful in discovering malarial parasites.

It is felt that by using a red filter the study for inclusion bodies of the Halberstädter-Prowazek type is facilitated. Routine studies can be made more rapidly. Less experienced observers can pick them up with great efficiency. Even the most experienced microscopist will occasionally miss an inclusion body when its background is conducive to that end. The filter unearths these evasive stigmas.

When, as occasionally happens, these bodies are limited to the nucleus of one cell on a slide, one can see how easily that cell could be missed. Lindner stated, ". . . . occasionally only one cell . . . with inclusions can be found in an entire specimen or even several smears."[4] That "one cell with inclusions" is of vast importance. The red filter may make it more visible.

349 Eastern Parkway (16).

7. Caries, R.: Rapid Diagnosis of Malaria by the Use of a Wratten Light Filter, J. Lab. & Clin. Med. **28**:1150, 1943.

OCCLUSION OF THE CILIORETINAL ARTERY

JESSE M. LEVITT, M.D.
BROOKLYN, N. Y.

IN CLOSURE of the central retinal artery, sparing of the macula with preservation of central vision due to the presence of a cilioretinal artery is a well recognized entity. The converse, closure of the cilioretinal artery with a normal functioning central retinal artery, has seldom been observed. Only 6 cases have been reported in the literature, and none within recent years. The main data in the reported cases are given in the accompanying table.

Summary of Reported Cases of Occlusion of Cilioretinal Artery, Including Present Case *

Author	Age, Yr.	Sex	Eye	Initial Vision	Initial Scotoma	Macula	Last Vision	Residual Scotoma
Hirsch, C.: Arch. f. Augenh. **33**: 139, 1896	31	M	R	Fingers at 4 meters	Cecocentral	Cherry red spot	6/6	Narrow band between fixation and blindspot
Zentmayer, W.: Ophth. Rec. **15**: 613, 1906	21	M	R	6/6	(No further record)			
Krauss, F.: Ophth. Rec. **16**: 196, 1907	18	F	R	5/30; eccentric	Cecocentral	Incomplete cherry red spot	5/4	Small paracentral
Meller, J.: Arch. f. Ophth. **72**: 456, 1909	35	F	L	Fingers at 1 meter	Central	Cherry red spot	6/36	Small central
Levy, A.: Tr. Soc. U. Kingdom **29**: 130, 1909	22	..	R	6/60	(No further record)			
Trappe, E.: Ztschr. f. Augenh. **32**: 124, 1914	16	°F	R	Fingers at 1.5 meter	Central 15-20°	Cherry red spot	5/50 eccentric	Central, 10°
Levitt	19	F	L	20/200	Cecocentral	Normal	20/15	Narrow band between fixation and blindspot

* In every case there was opacity of retina extending from near the temporal margin of the optic nerve up to or including the macular zone.

Closure of the cilioretinal artery is usually manifested by sudden loss of central vision. Young people are affected. The fundus presents a large band of retinal opacity extending from near the temporal margin of the optic nerve to or beyond the macula. A cherry red spot in the macula is a frequent finding. The margins of the optic nerve are slightly hazed, especially temporally. A cilioretinal artery is observed coursing through the affected portion of the retina. At the beginning the probable site of occlusion may be veiled by the edema, and with

Read before the Brooklyn Ophthalmological Society, Dec. 18, 1947.

subsidence of the edema a localized narrowing in caliber of the vessel may be made out. The peripheral field of vision is normal. A large scotoma corresponds to the area of involved retina and usually includes the fixation point. With the passage of weeks, the retina slowly regains its transparency, and the fundus in general is restored to normal. The scotoma becomes gradually smaller and is finally reduced to a narrow band between the fixation point and the blindspot. In some cases a central scotoma remains permanently. There is usually no adequate etiologic factor to explain the occurrence.

In the following case the typical changes associated with closure of the cilioretinal artery were observed in the left eye. The presence, in addition, of a cilioretinal vein in the right eye represented a rare finding.

REPORT OF A CASE

Mrs. J. R., aged 19, was first examined on Aug. 27, 1947. She stated that on August 25 she had a general physical examination at a department store prior to employment, and that the vision of each eye was recorded as 20/20. After the examination, a job which she did not like was offered to her, and she engaged in a heated argument. Later in the same day she received a letter from her mother-in-law which greatly disturbed her. At about 8 p. m., while she was sitting in front of her home, a shadow suddenly appeared over her left eye, and faces of people walking across the street were blotted out. The visual disturbance of the left eye was unchanged at the time of her first visit.

She had measles and mumps in childhood; she had never had any operations or serious illnesses. She had been married for three years and had a healthy boy 2 years of age. At the end of April 1945 she had a miscarriage, complicated by infection, and had had leukorrhea since.

Ocular examination (August 27) revealed vision of 20/15 in the right eye and 20/200 (unimproved) in the left eye. Jaeger type 1 was read with the right eye, but no print could be read with the left eye. External examination showed nothing remarkable. The pupillary reactions were unaltered. The media of both eyes were clear. The right fundus was free of pathologic change; a typical cilioretinal artery and a cilioretinal vein were present (fig. 1 *A*). The left fundus (fig. 1 *B*) showed a large band of snow white retinal opacity with festooned borders, extending from slightly temporal to the optic nerve to the margin of the macular zone. The optic disk was round and of good color, with a round, deep physiologic cup; and the temporal, upper and lower margins were slightly hazy. The macular zone was normal, with good macular and foveal reflexes. There were two typical cilioretinal arteries, one coursing in normal retina below the involved area and the other in the middle of the edematous retina and largely obscured by it. There was a large, aberrant macular vein along the upper margin of the opaque portion of the retina, coming from the macular zone and emptying directly into the superior retinal vein in the physiologic cup. Otherwise, the central retinal artery and vein and their subdivisions were normal, and macular vessels from the superior and inferior temporal arteries and veins arched around the macular zone in the usual manner.

The peripheral field of the left eye was normal. There was an absolute central scotoma in the left eye, demonstrated in the stereoscope with Haitz charts. Tests on the Evans scotometer with a 0.6 mm. white object, using binocular fixation, revealed a large scotoma (fig. 2 *A*) which included the enlarged blindspot and extended through the fixation point 4 degrees nasally below the horizontal meridian.

On the morning of the following day (August 28) vision in the left eye and the fundus picture were unchanged. In the afternoon an intravenous injection of 100 mg. of sodium nitrite was given and an effect was immediately visible. The aberrant macular vein became fuller and clearer to view. There was an appreciable lessening of the edema of the retina. The margins of the disk became clearer.

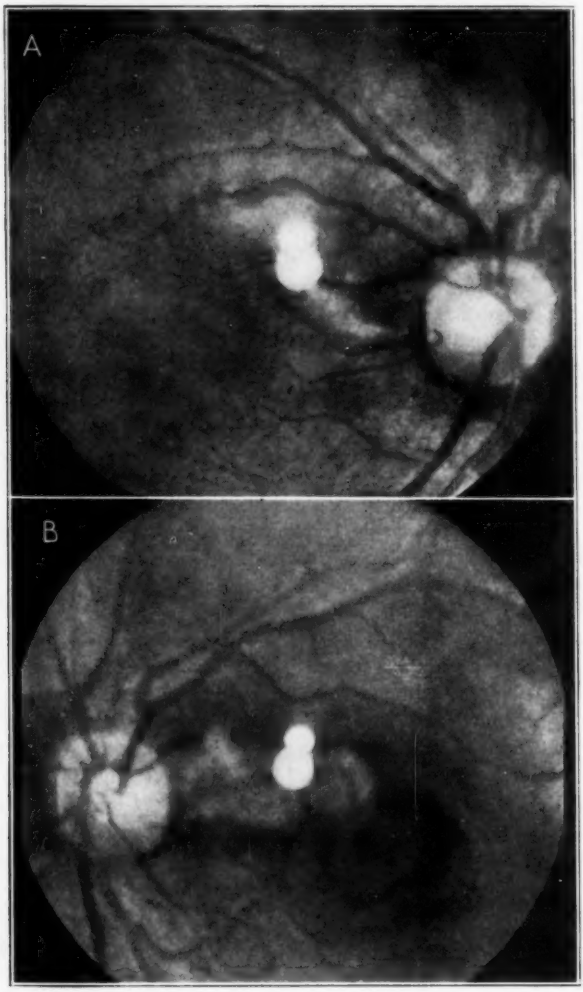


Fig. 1.—*A*, fundus of the right eye, showing cilioretinal artery and vein and an aberrant macular vein draining into the central retinal vein at the optic disk. *B*, fundus of the left eye, showing retinal edema between the optic nerve and the macula, an aberrant macular vein along the upper border of the edematous area, a cilioretinal artery within the area obscured by the edema, a second cilioretinal artery below the area and a normal macular zone.

The treatment consisted of eight daily intravenous injections of 100 mg. of sodium nitrite and the oral administration of 1 grain (0.065 Gm.) of erythrol tetranitrate and 500 mg. of nicotinic acid daily, in divided doses, for a month.

On August 29 vision in the left eye was 20/40 and the central scotoma had entirely vanished. On August 30 vision in the eye was 20/15 with Jaeger type 1 for near. On August 31, with lessening of the retinal edema, a tiny, triangular retinal hemorrhage was visible overlying the aberrant macular vein near the border of the disk, and in a week it had been entirely absorbed. The blurring of the margins of the disk disappeared entirely. The snow white retinal opacity slowly disappeared, and by September 25 the area had an almost normal appearance. The large scotoma slowly decreased in size, in correspondence with the decreasing size of the retinal lesion. A seeing area intervened between the blindspot and the scotoma. The blindspot returned to normal. A small scotoma between the blindspot and the fixation point (fig. 2*B*) remained as the only evidence of the vascular lesion. A narrowing in caliber of the cilioretinal artery,

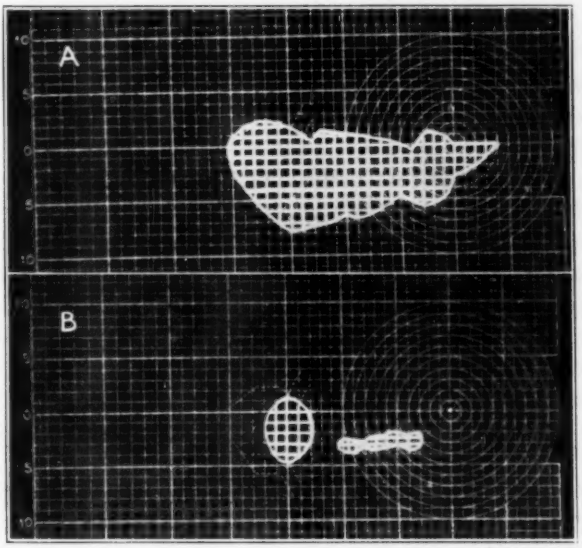


Fig. 2.—*A*, central field of vision in the eye (left) the fundus of which is pictured in figure 1 *B*. Vision was 20/200; the field was taken with a 0.6 mm. white test object on the Evans scotometer, using binocular fixation. *B*, central field of vision of the same eye taken with a 0.6 mm. white test object five weeks after onset, with fundus restored almost to normal and residual scotoma. Vision was 20/15; near vision, Jaeger type 1.

the probable site of the blockage, became evident near the margin of the disk with the lessening edema.

A complete survey for the cause was undertaken, without any significant factor being disclosed. General examination revealed nothing abnormal. The blood pressure was 120 systolic and 60 diastolic. Examination of the ears, nose and throat showed a normal condition. Gynecologic examination disclosed chronic cervicitis, with Trichomonas vaginalis as the infective organisms. Roentgenograms of the chest and teeth were normal. The electrocardiogram was normal. The Kolmer reaction of the blood was negative. The urine was normal. The Mantoux test gave a positive reaction to old tuberculin in 1: 10,000 dilution.

COMMENT

A quite similar clinical picture of retinal opacity may be seen in blockage of other vessels which supply the peripapillary and macular areas, such as a branch of the superior or the inferior temporal division of the central retinal artery, an aberrant macular artery coming directly from the central retinal artery or ciliary arteries other than the cilioretinal vessel. With blockage of a ciliary vessel, no visible vascular abnormality may be evident in the fundus on ophthalmoscopic examination. Knapp [1] observed 2 cases with retinal edema between the disk and and the macular zone without evident vascular abnormality; in both cases there was chronic cardiac disease, and he assumed that embolism of a ciliary artery near the optic nerve or in the choroid had occurred. Goldstein and Wexler [2] reported a similar observation in a case of arteriosclerosis and chronic lipid nephrosis, in which microscopic examination of the eye revealed emboli in the posterior ciliary arteries on the temporal side of the optic nerve, as well as in the central retinal artery.

It is quite probable that occlusion of a cilioretinal artery may occur without the patient being aware of it, particularly when the central vision is not affected and the vision of the other eye is good.

A discussion of the exact cause of the blockage, whether embolism, thrombosis, localized vascular disease or spasm, would, as in the case of closure of the central retinal artery, be fruitless. In most of the reported cases the origin was considered embolic. Vasospasm of psychogenic origin would seem to be the most logical explanation.

SUMMARY

The main observations in 6 cases reported in the literature and in an additional case of occlusion of the cilioretinal artery are tabulated.

The case is presented of a woman aged 19 with monocular loss of central vision; a broad band of retinal edema between the optic nerve and the macula, within which there was a localized constriction of a cilioretinal artery; a normal macular zone, and a large cecocentral scotoma. The fundus of the other eye showed a cilioretinal vein as well as a cilioretinal artery. No adequate cause of the disturbance was found on thorough investigation. Treatment consisted in intensive use of vasodilators. Almost complete recovery ensued. The fundus returned to a completely normal appearance, and only a narrow band scotoma between the blind-spot and the fixation point remained as evidence of the lesion.

991 Ocean Avenue.

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1. Knapp, H.: Ueber Verstopfung der Blutgefasse des Auges: Embolie der Ciliararterien, Arch. f. Ophth. **14**:237, 1868.

2. Goldstein, I., and Wexler, D.: Embolism of the Central Retinal and Ciliary Arteries, in a Case of Chronic Lipoid Nephrosis with Thrombosis of the Innominate Artery, Arch. Ophth. **10**:70 (July) 1933.

"SILENT" DACRYOCYSTITIS

FREDERICK H. THEODORE, M.D.
NEW YORK

THE PURPOSE of this paper is to call attention to a mild type of dacryocystitis, usually mucoid in character, which is often the unsuspected cause of persistent conjunctivitis, or of unexplained tearing. This clinical entity may be called the "silent" type of dacryocystitis. For the most part, the patients comprising the present series had been treated for long periods by conventional methods, without improvement. In almost every case the lacrimal sac had been declared normal because irrigation had revealed its patency. Yet when irrigation of the lacrimal passages was performed with the purpose of collecting and examining the washings, certain clinical and bacteriologic evidence was obtained indicating inflammation of the lacrimal sac. The clinical evidence consisted in mucus, mucopus or small amounts of frank pus in the collected fluid washed through the lacrimal passages. Bacteriologically, cultures of both the conjunctiva and the material in the washings usually revealed the same pathogenic organism, Staphylococcus aureus A or Staphylococcus albus A. Most of the patients had trouble with one eye only, and irrigation of the lacrimal passages of the uninvolved eye gave washings which were entirely clear. When treatment was directed toward eradication of the dacryocystitis, generally by frequent irrigations, the conjunctivitis, which in almost every case had existed for months, subsided in a matter of weeks, recovery paralleling the clearing of the lacrimal washings. When mucopus or frankly purulent material had first been encountered, pure mucus was seen before the washings became entirely clear. Nasal examination in almost every case showed a normal condition.

Since the general tendency of late has been to underestimate the value of conservative therapy of the lacrimal tract, interest in office procedures has waned to an undeserved extent. As a consequence, many ophthalmologists perform the irrigation of the lacrimal sac in such a manner as to miss much of the information obtainable. It appears customary to have the patient sit with his head tilted back, or to have him lie on his back, when irrigation is done. If the sac is patent, the fluid enters the throat through the nasopharynx. The only fact estab-

Read before the New York Society for Clinical Ophthalmology, March 3, 1947.
From the Ophthalmologic Service of Dr. Henry Minsky, the Mount Sinai Hospital.

lished is that the lacrimal passages are patent. Even the degree of patency cannot be estimated accurately; the resistance of the plunger is the only guide. In fact, even the diagnosis of patency may be incorrectly arrived at, should a nervous patient gag at the moment of irrigation. In any event, once patency is believed to be established, the sac is exonerated as normal and is forgotten. But the washings are lost, and the opportunity to study the contents is missed.

However, when the lacrimal passages are irrigated with the patient seated, head bowed, with the chin against the neck, the fluid will come out through the nose. In addition to the obvious preference on the part of the patient for a more comfortable experience, the following advantages make this technic most desirable:

1. The degree of patency can be noted by observing the rate of outflow. Thus, partial stenosis can be discovered and treated.

2. If the fluid is collected in a clean or sterile receptacle (preferably black), there may be noted the presence of fine shreds, clumps of pus or collections of mucus, indicative of inflammatory reaction in the lacrimal passages. The washings may be examined microscopically. Cultures and smears may be made. This approach is exactly that of the otolaryngologist when he suspects disease of the sinuses, especially the antrum. It is, of course, necessary to have the patient blow his nose and then to clean the inferior meatus with a moist swab before irrigation is performed, in order to be sure that nasal secretion is not mixed with the washings.

3. This method makes it possible for the ophthalmologist, in treating a stenosis or an infection, to irrigate with large quantities of fluid without causing the patient to gag or choke, and enables him better to judge the efficacy of his treatment.

The procedure of irrigation is facilitated if the ophthalmologist is also in a sitting position. The preliminary injection of cocaine and naphazoline ("privine") hydrochloride aids both in making the irrigation painless and in permitting the vasoconstriction to free those inflammatory products which might otherwise adhere to the mucosa and remain undiscovered.

The importance of examination of the washings is to be stressed especially. While many ophthalmologists irrigate in the manner suggested, they do not as a rule pay the particular attention to the character of the lacrimal washings which it deserves. Only Herman Knapp [1] has pointed out the full diagnostic value of irrigation of the sac, stating:

> . . . syringing is used: (1) for diagnostic purposes in obstructions and in inflammations: the purity of the escaping water or its admixture with other sub-

1. Knapp, H., in Norris, W. F., and Oliver, C. A.: System of Diseases of the Eye, Philadelphia, J. B. Lippincott Company, 1898, vol. 3, p. 897.

stances will aid in determining the nature of the inflammation, whether catarrhal, purulent or septic.

Fuchs [2] stressed the value of irrigating with the patient's head forward to determine patency, but did not comment on examination of the washings themselves.

There is little likelihood of confusing the washings from the sac with nasal secretion if the nose is cleansed before irrigation. Moreover, mucopus or shreds, when present, appear during the course of the washing usually only after some clear fluid has gone through. Mucus itself is generally not dislodged until the second 5 cc. of saline solution is used. To be sure that the sac is normal, therefore, at least 10 cc. of fluid must be injected. Furthermore, fluid from irrigation of the other sac is normal in each case, and, with subsequent irrigations of the involved side, the fluid becomes clearer as the condition improves. All these findings, in the absence of a pathologic condition of the nose, would substantiate the assumption that the abnormal washings come from the lacrimal passages.

REPORT OF CASES

Illustrative cases are described briefly.

CASE 1.—L. A., a man aged 52, first seen on May 11, 1946, had had severe catarrhal conjunctivitis in his right eye for over six months, the infection following a chalazion three months previously. He had become sensitive to penicillin and sulfonamide drugs. In addition to the conjunctivitis, examination revealed meibomitis. Externally, the lacrimal sac appeared normal. Pressure over the sac yielded no discharge. On irrigation, however, a large "icicle" of mucus appeared from the right nostril, after clear water had first come through. Cultures both of material from the conjunctiva and of the mucus revealed toxic Staph. albus (mannitol fermenting). Irrigation was with large quantities of benzalkonium ("zephiran") chloride and saline solution. His condition had improved so much after the first treatment that he requested irrigation when he next returned. Irrigation was therefore repeated at weekly intervals. Although two months later a slight amount of mucus still remained in the sac, the conjunctiva was entirely normal. Otolaryngologic consultation revealed no pathologic condition of the nose.

CASE 2.—R. M., a woman aged 80, seen on Oct. 18, 1946, had been treated seven months for severe follicular conjunctivitis of the right eye. The sac had been irrigated previously and declared normal. Irrigation with the patient's head forward revealed stenosis of the lacrimal passages and a "glob" of pus in the lacrimal washings. Cultures of secretions from the conjunctiva and of the pus both showed Staph. aureus A. Smears showed staphylococci. On irrigation with penicillin, in a concentration of 1,000 units per cubic centimeter, the pus disappeared from the washings, to be followed by a considerable amount of mucus. The conjunctiva became normal in three and one-half weeks, but a small amount of mucus was still present in the lacrimal washings.

2. Fuchs, E.: Text-Book of Ophthalmology, translated by A. Duane, ed. 8, Philadelphia, J. B. Lippincott Company, 1924, p. 515.

CASE 3.—L. M., a man aged 59, first seen on June 7, 1946, had had low grade papillary conjunctivitis in the right eye for five months. The lacrimal sac had been irrigated successfully and declared normal, despite the fact that tearing was his major complaint. He had used antibiotics, with indifferent success. Irrigation revealed mucopus in the washings. Culture of material from the conjunctiva and of the pus showed a few colonies of Staph. aureus A. Irrigations with penicillin were instituted, and washings became clearer in a short time, along with subsidence of the conjunctivitis.

CASE 4.—M. R., a boy aged 14, first seen on Oct. 12, 1946, with a history of severe sinusitis, complained of tearing in the right eye for about six months. The conjunctiva was moderately injected. Irrigation of the lacrimal passages showed patency, but toward the end of the irrigation a considerable amount of mucus appeared. Control irrigation of the passages on the left side yielded clear fluid. Because it was felt that the associated pathologic condition of the nose was the cause of the dacryocystitis, the patient was treated by an otolaryngologist for several months. Irrigation of the lacrimal passages at that time still yielded flakes and mucus, but less than before. His tearing, having diminished considerably, hardly bothered him. In this case, the mucous dacryocystitis was probably due to an extension from the nasal cavity, and improvement occurred after treatment of the nasal sinuses.

CASE 5.—I. B., a nurse aged 43, was first seen on Jan. 24, 1947. In 1936, after bilateral conjunctivitis, an overwhelming infection of the right eye with Staph. aureus had occurred by direct extension, necessitating evisceration. For the four months prior to consultation she had complained of inflammation of the left eye. Examination revealed moderately severe papillary conjunctivitis with some puffiness of the margins of the lids. Cultures of material from the lid margins and conjunctiva showed nontoxic Staph. albus B. Irrigation of the lacrimal passages was productive of considerable mucus. Cultures of this mucus and the nasal secretion both yielded Staph. albus A, toxic variety. The sac was treated with irrigations of penicillin, in a concentration of 15,000 units per cubic centimeter, together with subcutaneous injections of staphylococcus toxoid and the conjunctival instillation of drops of sodium sulfacetimide and naphazoline ("privine") hydrochloride. The lacrimal washings cleared within a month, but the conjunctiva did not improve significantly until several months later. At the time of writing, the sinusitis, probably the cause of the mucous dacryocystitis, remains unchanged. She still receives nasal treatment regularly. The past history suggests a low resistance to the staphylococcus.

CASE 6.—D. B., a man aged 40, first seen on March 21, 1947, complained of tearing in both eyes for several years. The conjunctiva did not appear significantly inflamed. Irrigation of the right lacrimal passages was productive of a moderate amount of mucus; washings from the left lacrimal passages were clear, although stenosis was present. Subsequent irrigations gave clear washings from both sides, and tearing ceased in three weeks.

CASE 7.—Despite the fact that involvement of the lacrimal sac was obvious from the history alone, this rather unusual case is included because it illustrates the value of investigating the lacrimal washings in all cases of disease of the lacrimal sac. A clerk, aged 34, was seen on Nov. 20, 1945, because of severe tearing of the left eye for the previous week. The conjunctiva was normal. Only after irrigation with considerable force did a fine trickling of clear water come through. The next day, probing revealed a strong, boggy obstruction at the lower

end of the sac. When the probe was withdrawn, pus oozed through the punctum. Culture and smear of this pus showed pneumococci. A no. 3 probe was then passed to the nose, and penicillin was injected into the sac. The course of the dacryocystitis in this case may be described in four stages: (1) incomplete obstruction by an abscess-like inflammation of the mucosa; (2) drainage of the abscess, characterized by frank pus in the lacrimal washings; (3) improvement, characterized by decreasing amounts of pus and increasing amounts of mucus, and (4) resolution, characterized by the presence of mucus without pus, followed by the absence of both mucus and pus and the relief of tearing.

COMMENT

Dacryocystitis is generally described in the ophthalmic literature as a chronic inflammation of the lacrimal sac due to stenosis of the nasolacrimal duct, which usually is of considerable degree, if not complete. The stenosis, in its turn, develops as a result of inflammation of the nasal mucosa extending by continuity to the mucous membrane of the nasolacrimal duct. A mucopurulent or purulent discharge is present, which flows into the conjunctival sac on pressure. Sometimes a mucocele develops in cases of long-standing disease. The condition known as acute dacryocystitis is more properly designated as acute peridacryocystitis; it occurs when the organisms present in chronic dacryocystitis penetrate the submucous tissue and invade the wall of the sac itself. Thus, the "acute" inflammation is secondary to chronic dacryocystitis. These two obvious types of inflammation of the lacrimal sac appear to be the only ones generally accepted. A third type seems to deserve inclusion in the everyday thinking of the ophthalmologist.

It is not sufficiently recognized that there exists an incipient, mild, low grade dacryocystitis in which obstruction does not play an obvious role. Experience would indicate, however, that such a "silent" dacryocystitis is by no means rare, but, on the contrary, is often discovered when looked for in likely cases. If this more or less acute, although mild, dacryocystitis does not clear up, it is possible that the classic chronic type of dacryocystitis may result. It is only logical to assume that the mucous membrane of the lacrimal sac, like mucous membrane elsewhere, containing mucous cells, and sometimes mucous glands, is susceptible to mild, sometimes transient, inflammations. In cases of this type only mucus would be found. Furthermore, in the severer inflammations, in which a purulent or mucopurulent exudate occurs at first, only mucus might be noted later. The lacrimal washings in the cases reported here indicate that as the inflammation subsides mucus is always found sooner or later, before cure is complete. Thus, the presence of mucus may indicate either mild inflammation per se or an intermediate stage in the course of a severer dacryocystitis. Associated nasal disease may, of course, be present; it may even be the cause of the dacryocystitis. The important point is that early evidence of

dacryocystitis causing conjunctivitis, or only tearing, may be discovered and the condition adequately treated if the systematic examination of the eye includes the technic described here—qualitative and quantitative inspection of the washings resulting from irrigation of the lacrimal passages.

SUMMARY

A mild type of dacryocystitis, usually mucoid in character, is often the unsuspected cause of persistent conjunctivitis or of unexplained tearing. This "silent" type of dacryocystitis is overlooked if investigation of the tear passages is limited only to a determination of patency. If, however, the lacrimal washings are collected and examined both clinically and bacteriologically, the finding of mucus, mucopus or frank pus containing pathogenic bacteria will indicate the presence of "silent" dacryocystitis. In cases of this type obstruction does not play an obvious role. Once the diagnosis is established and treatment of the dacryocystitis instituted, the conjunctivitis, which in almost every case of the present series had existed for months, subsided in a matter of weeks, recovery paralleling the clearing of the lacrimal washings. Experience suggests that this low grade type of mucous dacryocystitis is not uncommon and, if not recognized, may eventually lead to more obvious inflammatory changes in the lacrimal passages.

667 Madison Avenue (21).

THE HISTORY OF THE DARTMOUTH EYE INSTITUTE

HERMANN M. BURIAN, M.D.
BOSTON

THE DARTMOUTH Eye Institute, of Hanover, N. H., has closed its doors. A unique institution has passed from the scene of American ophthalmology. It is worth while looking at its history.

The origin of what in 1937 became the Dartmouth Eye Institute dates back to 1919. In that year Adelbert Ames Jr. came to Hanover, N. H., to join with Prof. Charles Proctor, of the department of physics of Dartmouth College, in carrying out research on the optical properties of the human eye.

Ames is neither an ophthalmologist nor a physicist. Trained as a lawyer, he abandoned law to become an artist. Being of an analytic as well as artistic temperament, he soon became interested in the question of the relation of what one sees to what is represented on the canvas. The pursuit of this problem led to the question how the organ of sight reproduces the environment. In other words, Ames became interested in the relation of objective and subjective space.

Ames felt that to answer this broadest question he had to begin at the beginning, and he decided to investigate the problem of the image formation in the eye. This brought him to Hanover and led to the excellent studies by Ames and Proctor on the dioptrics of the eye,[1] and to the establishment of the Department for Research in Physiologic Optics.

The practical purpose of the study of the aberrations in the human eye was to construct an optical instrument, a camera, which would duplicate as closely as possible the image formation in the human eye. It was hoped that such an instrument would contribute further knowledge to the question of how one sees.

The help of Gordon H. Gliddon, of the lens-designing division of the Eastman Kodak Company, was enlisted in the construction of the camera.[2] He remained until 1936 closely associated with the research work of Mr. Ames. After that, until 1945, he was engaged in work of administrative nature at the Dartmouth Eye Institute.

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1. Ames, A., Jr., and Proctor, C. A.: Dioptrics of the Eye, J. Optic. Soc. America **5**:22-84 (Jan.) 1921.

2. Gliddon, G. H.: An Optical Replica of the Human Eye for the Study of the Retinal Image, Arch. Ophth. **2**:138-163 (Aug.) 1929.

It was soon found that further examination of the optical properties of the single eye would not advance materially the solution of the basic problem. Ames then began to tackle the question of binocular vision on a broad basis, leading off with one of the most complicated factors, cyclophoria, which he dealt with in an exhaustive experimental study.[3]

It was at this point that the work of Ames first came to the attention of ophthalmologists. More especially, Walter B. Lancaster, of Boston, became interested in the studies carried on at Dartmouth and lent his active help and advice. This became all the more important since the study of the physiology of vision necessarily brought about a consideration of anomalies of vision, the handling of clinical cases. The first fruit of measurements on persons with ocular anomalies was the construction of a device for the correction of cyclophoria in near vision. This device was published by Lancaster in a clinical report.[4]

Concurrently with the study of cyclophoria, Ames and Gliddon carried out an ambitious program of study of visual physiology, covering in careful measurements accommodation, astigmatism, horizontal and vertical heterophoria, and cyclophoria.[5] Not only were these measurements performed on a modified haploscope, uncommonly precise; the authors also discovered a number of interesting phenomena. Among them was the first indication of what was to become the most important contribution to clinical ophthalmology made by Ames and his co-workers, namely, the existence and significance of retinal asymmetries.

This particular subject was followed and studied relentlessly in the ensuing years; finally, in 1932, a series of papers were published in which the physiologic and clinical significance of the anomalies in the size and shape of the ocular images was discussed and in which the methods of measurement and of correction were presented. These papers laid the foundation for knowledge of what came to be known as aniseikonia.

It has been appreciated for a long time that a large difference in the ocular images (such as exists in the extreme cases of corrected refractive anisometropia) may present an insuperable obstacle to fusion. But it had never been considered that small relative image size differences, of the magnitude of 0.5 to 2 per cent, may create such difficulties for the fusion apparatus that the person afflicted with this condition may experience symptoms of asthenopia not accounted for by other ocular anomalies or relieved by their treatment when they are present. It was

3. Ames, A., Jr.: Cyclophoria, Am. J. Physiol. Optics **7**:3-38 (Jan.) 1926.

4. Lancaster, W. B.: The Ames Spectacle Device for the Treatment of Cyclophoria with a Report of a Successful Case, Arch. Ophth. **57**:332-338 (April) 1928.

5. Ames, A., Jr., and Gliddon, G. H.: Ocular Measurements, Tr. Sect. Ophth., A. M. A., 1928, pp. 1-68.

Ames who not only discovered this fact but studied with his co-workers the different types of possible retinal asymmetries, elucidated their physiologic and clinical significance, devised methods for their detection and measurement and for their correction and, with rare single-mindedness, insisted that aniseikonia be recognized as a clinical entity requiring measurement and correction.

But aniseikonia is not only an obstacle to fusion. Within the limits in which binocular vision is possible in the presence of an aniseikonia, it has a profound influence on spatial orientation as determined by stereopsis. This was noted at an early date by Ames and was studied thoroughly (with regard to aniseikonia in the horizontal meridian). As a means for this study, the empiric longitudinal horopter was employed. These investigations [6] were far more than a mere application of horopter measurements to problems of aniseikonia; they represent a significant contribution to the horopter problem in general. This is particularly true of the outgrowth of this work, the analytic treatment of the curve of the empiric longitudinal horopter by Ogle,[7] who had in the meantime joined the department, first as a graduate student and then as a full-fledged member.

The years following the publication of these papers were devoted to the further development of the methods of measuring and correcting aniseikonia. Patients, referred from various parts of the country, began to arrive, and the clinical end of the department was built up. It was joined by an ophthalmologist, Dr. Elmer H. Carleton, and an optometrist, Leo F. Madigan.

The more these clinical studies progressed, the more the feeling grew that aniseikonia, as a component of the sensory part of the visual apparatus, has a significant bearing on the neuromuscular anomalies of the eyes. It was at this time that Alfred Bielschowsky, of Breslau, Germany, visited this country as a lecturer. Lancaster, always maintaining his interest in the work of Ames, suggested to him that Bielschowsky might be willing to come to Hanover to join the department. Ames approached Bielschowsky, and he agreed to come for a six months' visit. During this visit he became so impressed with the possibilities which the department had to offer that he decided to return to Hanover to stay permanently.

The coming of Bielschowsky gave a tremendous impetus to the organization. The Department of Research in Physiological Optics

6. Ames, A., Jr.; Ogle, K. N., and Gliddon, G. H.: Corresponding Retinal Points, the Horopter and Size and Shape of Ocular Images, J. Optic. Soc. America **22**:538-578 (Oct.); 575-632 (Nov.) 1932.

7. Ogle, K. N.: An Analytical Treatment of the Longitudinal Horopter: Its Measurement and Application to Related Phenomena, Especially to the Relative Size of the Ocular Images, J. Optic. Soc. America **22**:665-728 (Dec.) 1932.

was transformed into the Dartmouth Eye Institute, consisting of a research division and a clinical division. A new grant was obtained from the Rockefeller Foundation, which had in the past generously supported the work.

Bielschowsky became director of the Institute, and the staff of each division was enlarged considerably. The work of the clinical divisions, more especially, was expanded. Its medical members were granted the privileges of the staff of the Mary Hitchcock Memorial Hospital, and in the course of time the Dartmouth Eye Institute became a well regarded center of ophthalmic work in Northern New England.

As was natural with the foremost authority on ocular motility at the head of the institution, this field of ophthalmology was particularly cultivated. But there was also a close association of the clinical with the research division, and all members engaged in active research, prevalently concerned with the physiology and pathology of binocular vision and with the physiopathologic basis of the neuromuscular anomalies of the eyes. The research division continued to carry on its problems: Ames became more and more interested in the problems regarding aniseikonia and spatial orientation and its influence on the functioning of the organism; Ogle worked on refinement of the means of measuring and correcting aniseikonia and on what became known as the "induced" size effect.

In addition to all this work, the members, under the active leadership of Bielschowsky, attended numerous meetings, both ophthalmologic and optometric, gave papers and lectures and, more especially, had regular monthly gatherings at the Institute, which were well attended by ophthalmologists from New Hampshire, as well as the neighboring states, and which represented a sort of continuous informal postgraduate course in ophthalmology.

The sudden, and most untimely, death of Bielschowsky in January 1940 was a severe blow to all these activities. He was not immediately replaced by a successor, and the writer of this note attempted to carry on the responsibilities of the clinical division on an informal basis, a rather difficult task, in view of the lack of official authority to do so.

To the great relief and joy of all members of the staff, Walter B. Lancaster agreed in the fall of 1940 to head up the Dartmouth Eye Institute. He had for the preceding twenty years shown the greatest interest in its work; he had at all times actively assisted in the work with his advice; he had many times in meetings of various ophthalmologic groups placed his great authority behind the work of Ames, in the face of severe criticism of that work. It was felt by the staff that his knowledge of the field, his intimate acquaintance with the organization and traditions of American ophthalmology, the weight of his word with those best qualified in the field and, last but not least, his

inspiring personality not only would give a new and better standing to the Dartmouth Eye Institute in the medical world but also would bring its work to a new flowering under his leadership.

Unfortunately, this was not to be so. Lancaster had tacitly understood that he was to be the director of the Institute and that he would, as such, have a decisive influence on its policies. But when he came, he found that a reorganization had taken place. The director was now a layman, originally appointed by the president of Dartmouth College to raise funds for the Dartmouth Eye Institute and improve its administration, which had been run in a somewhat amateurish fashion. The policies were to be determined by a board of trustees, on which the medical members of the Institute had no influence. Lancaster himself was given the title of chief of staff. Not one to be deterred by the matter of a title, Lancaster, in spite of this disappointment, nevertheless went to work with amazing energy, trying to put his ideas to work. But he soon found that this was by no means easy. In the general policies of the Institute his word had little weight; he could do little to influence the direction of the research work, and even in the running of the clinical division he was often thwarted. It was especially painful to him that his cherished plan of developing the Dartmouth Eye Institute as a teaching institution—for which it was eminently suited—was absolutely declined. Lancaster worked and fought hard for what he had come to achieve at a considerable personal sacrifice. But, finally, he drew the only possible conclusion consistent with his dignity. In November 1942 he resigned and returned to his practice in Boston.

To every clear-sighted member of the staff it was obvious that it was the end of the Dartmouth Eye Institute when Lancaster was permitted to leave. Yet it seemed that this institution should not be left to disintegrate if it was at all possible. I was one who hoped against hope that it might be saved. I stayed on in the capacity of ophthalmologist in chief until July 1945, but it was a losing fight. Too many divergent interests prevented integrated progress. One after another, the members of the staff resigned. Various attempts at reorganization were unsuccessful; finally, in an announcement dated May 10, 1947, the closing of the Dartmouth Eye Institute was officially announced.

In spite of all the difficulties, the work continued through the years at the Institute. Its chief scope remained the field of binocular vision, aniseikonia and neuromuscular anomalies, although individual members contributed work outside these fields. The coming of Lancaster to the Institute brought renewed interest in refraction and some surgical technics, which found expression in papers published on these subjects.

Ames himself turned more and more to problems of a broader scope. He asked himself what significance the normal and abnormal, monocular

and binocular reactions have for the organism as a whole, and how they affect the functioning of the organism in space. From this he moved on to generalizations about the nature and origin of sensations and came to the conclusion that "the processes which underlie our perception of our immediate external world and those that underlie our perception of social relationships are fundamentally the same" and that "the insights gained in the study of visual sensation can serve as indispensable leads to better understanding and more effective handling of the complexities of social relationships." [8] Ames's investigations along these lines have as yet not appeared in print.

Every one who came in close contact with the Dartmouth Eye Institute was much impressed by the quality of the research and clinical work done there, but even more by the loyalty of the patients and the devotion to the Institute of the members of the staff. It is only just that one should ask, "Why did it have to close; why did it not last?"

As usual, the causes were multiple. The most important ones, as they appear to me, shall be mentioned.

The roots of the trouble go back very far. When aniseikonia was first presented to ophthalmologists, serious objections were raised by the leaders of the medical profession. These were never properly answered. Instead, exaggerated claims for aniseikonia were made which could not be substantiated. The cool reception by the members of the profession led, in turn, to an exaggerated sensitivity toward criticism, and an approach to less critical laymen was made in person or through the press which could not be approved by the members of the medical profession, either within or outside the Institute.

Except for a brief period during Bielschowsky's lifetime, no medical man within the staff had a significant influence on the policies or the running of the Institute. On the part of the research division, there was always expressed the fear that if such influence were established research might be made the handmaiden of the clinic, a fear which was totally unjustified. The potentialities of the Dartmouth Eye Institute as a center for research in physiology of vision, as an ophthalmic center for clinical work and clinical research and as a center for teaching were enormous. But every attempt on the part of medical members of the staff to realize these potentialities remained fruitless. They were always told that what they attempted to do was not what the Institute was for. Its only purpose was said to be to implement the work of Ames.

Ames, however, had actually lost his interest in the active work of the Institute, especially its clinical division. To him, the experimental

8. Ames, A., Jr.: Sensations, Their Nature and Origin: Brief Statement of the Findings of the Dartmouth Eye Institute, Hanover, N. H., Dartmouth Eye Institute, 1945.

work in physiologic optics had long since become a means for much broader purposes. He has always been imbued with that fine humanitarian spirit that has forever pervaded the best minds of New England. Essentially never a "scientist" in the academic sense of the word, he became increasingly impatient of the plodding and painstaking work in the laboratory and totally disinterested in the strictly ophthalmologic aspects of the work of the Institute. He turned increasingly to the philosophic and social implications of the work, as he saw it. Members of both the research and the clinical division regretted this exclusive preoccupation. Those who knew of the fabulous abilities of Ames as an experimenter, of his brilliant ideas in the field of visual physiology, could not help regretting that he had so largely abandoned this work as too narrow in scope. If they expressed their regret, they were rebuked for lacking breadth of vision. Thus the tension grew, and it became increasingly evident that the future which some members of the staff had envisaged for the Institute would never materialize. Reluctantly, one by one drew this conclusion.

So the Dartmouth Eye Institute ended. To those who were closely associated with it, and who had hoped for a brilliant future for it, this is a saddening end. But even to those who are only superficially acquainted with its work, it is evident that its closing is a great loss to scientific ophthalmology. The places are all too few in which the physiology of vision is competently cultivated. In the short span of its existence, the Dartmouth Eye Institute has made lasting contributions to this field. Its closing has nipped in the bud a great many promises.

A complete bibliography of the papers published by the members of the Dartmouth Eye Institute is appended.

520 Commonwealth Avenue (15).

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DI-ISOPROPYL FLUOROPHOSPHATE (D F P) IN TREATMENT OF GLAUCOMA

Further Observations

IRVING H. LEOPOLD, M.D.
AND
P. ROBB McDONALD, M.D.
PHILADELPHIA

DI-ISOPROPYL fluorophosphate (DFP) has been shown to have a marked and prolonged miotic effect in normal [1] and in glaucomatous eyes.[1b] It has been shown to lower intraocular tension in these eyes. Furthermore, there is evidence that these effects are brought about entirely by inactivation of cholinesterase, and not by direct action on the iris and ciliary muscle.[2] Although in this respect the pharmacologic effects of DFP resemble those of physostigmine and neostigmine, the DFP–cholinesterase combination is an irreversible one.[3] None of the methods successfully employed to split physostigmine and cholinesterase will break down this combination. Because of these properties of DFP and, more especially, because of the prolonged effect of very dilute preparations when locally applied to the normal eye, this drug was tested for its efficacy in the therapy of glaucoma.[1b]

The D F P used for these experiments was supplied by Merck & Co., Inc., Rahway, N. J.

From the Department of Ophthalmology, Hospital of the University of Pennsylvania, and Wills Hospital.

Read before the Section on Ophthalmology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 24, 1948.

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The initial studies indicated that DFP in 0.05 and 0.1 per cent concentrations in peanut oil could successfully lower intraocular tension in glaucomatous eyes and that its length of action was greater than that of previously employed miotics. In addition, these early studies suggested that DFP might be effective in some glaucomatous eyes when other miotics in the usually recommended concentrations had failed. Subsequent favorable reports on the use of DFP have been made by McDonald,[4] Lebensohn,[5] Haas,[6] Dunphy[7] and von Sallmann.[8] The least favorable results were those of Marr,[9] who found that only 1 of every 6 glaucomatous eyes in which the disease could not be controlled by other miotics could be held in normal tension by DFP for four months or longer. Dunphy[7] reported that DFP was successful in approximately 1 of every 3 eyes with chronic glaucoma that had failed to respond to other miotics. These studies were all on small series of patients who were observed for six months to one year. Therefore, it seemed advisable to determine the efficacy of DFP when observed in a large group for a longer period.

METHOD

Three hundred and seventy eyes of 252 patients with glaucoma in one or both eyes were tested with DFP during a period of thirty-seven months. In almost every case other miotic agents were tried before DFP was used. Tensions were estimated with a Schiøtz tonometer, tetracaine hydrochloride U. S. P. (0.5 per cent) being used for topical anesthesia. Visual acuities and visual fields were checked at regular intervals. All eyes were examined with a gonioscopic lens, and attempts were made to classify them on the basis of a wide or a narrow angle. Only in eyes in which the tension was maintained at or below 30 mm. of mercury and in which no loss of visual fields occurred for a period greater than four months was the glaucoma considered controlled.

DFP was diluted in peanut oil and in liquid petrolatum U. S. P. The concentrations employed were 0.01, 0.025, 0.05 and 0.1 per cent. Other miotics employed were physostigmine, both the salicylate and the sulfate, in 0.25 to 1 per cent concentration; pilocarpine nitrate, in 1 to 6 per cent concentration; combinations of pilocarpine and physostigmine; neostigmine hydrobromide, 5 per cent, with methacholine chloride U. S. P. (mecholyl chloride[R]), 20 per cent, and furfuryl

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trimethylammonium iodide (furmethide [R]), 10 per cent. In over 300 eyes more than one miotic other than D F P was tried; as many as five different miotics were tried in some eyes.

RESULTS

The results are summarized in table 1. In 116 of the 263 eyes with the chronic type of glaucoma, no miotic tried lowered the tension below 30 mm. of mercury for a four month period. Of the remaining 147 eyes, 77 were benefited by other miotics and DFP. In 70 eyes DFP successfully lowered the tension for at least four months after other miotics had failed; that is, in 26 per cent of all the eyes (1 of every 4 eyes) with chronic simple glaucoma in which the disease was not controlled by other miotics, it was controlled by DFP. The results in cases of narrow angle glaucoma were better than those in cases of the wide angle type.

TABLE 1.—*Comparison of Results of Treatment of Eyes with Various Types of Glaucoma by Means of D F P and Other Miotics*

Type of Glaucoma	Number of Eyes	Eyes Benefited by Other Miotics *	Eyes Benefited by DFP
Chronic glaucoma			
Wide angle	235	74	127
Narrow angle	28	3	20
Acute glaucoma	14	2	8
Secondary glaucoma			
Aphakia	53	8	39
Uveitis	18	2	11
Thrombosis of central retinal vein	6	0	0
Exfoliating lens capsule	1	0	1
Buphthalmos	4	0	2
Absolute glaucoma	7	0	0
Juvenile glaucoma	2	0	0
Intraocular growth	2	0	0
Total	370	89	208
Per cent of eyes controlled		24.05	53.5

* Tension 30 mm. of mercury or below (Schiøtz).

Of the eyes with acute glaucoma, D F P was successful in lowering the tension below 30 mm. of mercury in 42 per cent in which the disease was not controlled by other miotics. Of the eyes with aphakic glaucoma, DFP lowered the tension below 30 mm. of mercury in 31 (58.4 per cent) of the eyes in which it was not reduced by other miotics. In 50 per cent of the eyes with glaucoma secondary to uveitis, DFP lowered the tension satisfactorily where other miotics had failed. DFP was not successful in cases of absolute glaucoma or of glaucoma secondary to venous thrombosis or intraocular growth. It failed in 2 eyes with juvenile glaucoma. It maintained an acceptable tension for four months in 1 eye with an exfoliating capsule of the lens and in 2 eyes with

buphthalmos. Of the total 370 eyes, 24 per cent were benefited by other miotics and 53 per cent by DFP. When the 89 eyes benefited by other miotics were excluded, DFP was found to have been successful in 119, or 42 per cent, of the remaining 281 eyes.

In table 2 is indicated the length of time that DFP maintained the tension and visual fields in 189 eyes with chronic glaucoma, buphthalmos and exfoliating lens capsule. Only those eyes in which the tension was controlled for four months or longer were listed as benefited in table 1. In 83 eyes the disease has been controlled over one year; in 33, over two years, and in 5, three years. In 38 of these eyes resistance to the

TABLE 2.—*Duration of Therapy*

Number of Months	Number of Eyes Controlled by DFP
Less than 3 *	70
4-6	53
6-12	53
12-18	28
18-24	22
24-30	28
30-36	1
36+	4

* Eyes in which glaucoma was controlled for less than three months are not considered as controlled in table 1.

TABLE 3.—*Comparison of Effect of Miotics on Glaucomatous Eyes in Which Surgical Measures Against Glaucoma Had Failed*

Number of Surgically Treated Eyes	Number of Previous Unsuccessful Operations for Glaucoma	Eyes Benefited by DFP	Eyes Benefited by Previous Miotic
88	1	38	19
13	2	7	3
12	3	3	0
5	4	3	1
118		51	23

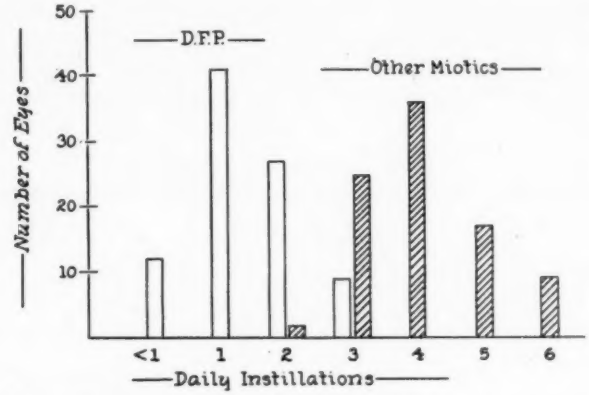
tension-lowering properties of DFP developed at varying times during the first year. The miotic properties, however, were not noticeably effected.

In table 3 are compared the effects of miotics on glaucomatous eyes in which surgical treatment had failed. Of 88 eyes in which one operation for glaucoma had been unsuccessful, 19, or 21 per cent, were controlled by other miotics and 43 per cent were controlled by DFP; of the 30 eyes operated on unsuccessfully two, three or four times, only 4 responded to other miotics, whereas 13 were controlled by DFP.

In the chart are compared the frequency of instillation of DFP and that of other miotics required to control the intraocular tension

in glaucomatous eyes in which it was successfully controlled by other miotics as well as DFP. It is evident that notably fewer instillations of DFP were required.

Table 4 lists the miotics which were unsuccessful in controlling tension in the eyes in which D F P was effective. It is evident that D F P



Comparison of the number of instillations of D F P and of other miotics required to control the intraocular tension in the same (89) eyes.

TABLE 4.—*Miotics Unsuccessfully Employed in Glaucomatous Eyes Controlled by D F P*

Miotic Unsuccessfully Used	Type of Glaucoma		
	Chronic Glaucoma	Aphakic Glaucoma, No. of Eyes	Acute Glaucoma, No. of Eyes
Pilocarpine nitrate, 1%	4	..	..
Pilocarpine nitrate, 3%	5	5	..
Pilocarpine nitrate, 6%	8	..	3
Pilocarpine nitrate, 1%, and physostigmine salicylate, 0.25%	14	..	..
Pilocarpine nitrate, 1%, and physostigmine salicylate, 0.5%	12	10	..
Pilocarpine nitrate, 2%, and physostigmine salicylate, 0.5%	8	8	..
Pilocarpine nitrate, 2%, and physostigmine salicylate, 1%	2	..	..
Physostigmine salicylate, 1%	5	4	1
Neostigmine hydrobromide, 5%, plus methacholine chloride, 20%	13	8	6
"Furmethide" hydrobromide, 10%	10	4	3

was able to lower tension for at least four months in eyes not controlled by 1 to 6 per cent pilocarpine nitrate, 1 to 2 per cent pilocarpine nitrate with 0.25 to 0.5 per cent physostigmine salicylate or sulfate, 5 per cent neostigmine hydrobromide with 20 per cent methacholine chloride, or 10 per cent furmethide.[R]

Table 5 reveals the concentrations of DFP employed in the eyes controlled by the drug. Although a few eyes responded to concentrations as low as 0.01 per cent, the majority required a concentration of 0.05 or 0.1 per cent.

In this series, 14 eyes in which the tension was not controlled by any previous miotic were treated with DFP, with interesting results. In every case the tension was lowered with DFP, though in 4 cases the medication was discontinued within three months, so that the disease in these eyes was considered uncontrolled. In the others, DFP was used with successful results from four to twelve months, but was then discontinued. The interesting feature is that in all these eyes the tension was subsequently controlled by other miotics or became normal with no miotic at all. In 1 eye the tension was controlled by 10 per cent furmethide [R] used six times a day; in 3, by 3 per cent pilocarpine nitrate used five times a day; in 4 by 0.5 per cent physostigmine

TABLE 5.—*Concentration of D F P Solution in Peanut Oil Employed in Control of Intraocular Tension*

Concentration in Peanut Oil, per Cent	Number of Eyes Controlled
0.01	4
0.02	15
0.05	86
0.1	103

salicylate or sulfate and 1 per cent pilocarpine nitrate, used four times a day, and in 4, with no miotic at all. In the last group, 3 of the 4 eyes had aphakic glaucoma, though there was no question that the patients had glaucoma, since they had been treated for some time prior to the institution of DFP therapy. One explanation of this may be that DFP, through its strong miotic effect, may have broken some peripheral anterior synechias and thus cleared part of the angle. It is also possible that in the cases of aphakic glaucoma a low grade uveitis subsided, with accompanying improvement in intraocular tension, so that miotics were no longer required.

When liquid petrolatum and peanut oil as vehicles were compared in the same eyes, better results were always obtained with the peanut oil preparations. DFP was poorly soluble in liquid petrolatum and frequently came out of solution. Dilutions of DFP were stored for fourteen months at room temperature and then compared clinically with freshly made solutions of the drug. The solutions were used in 20 eyes with chronic glaucoma; in every instance the aged dilutions were as effective in lowering and maintaining the tension as the fresh solutions.

DFP in peanut oil has been shown to be capable of storage for one year at room temperature without loss of anticholinesterase activity and to withstand autoclaving at 117 C.[3a]

COMMENT

From this study, and from previous ones, there is no doubt that DFP lowers intraocular tension in glaucomatous eyes. It is further evident that DFP has a longer duration of action than any miotic previously employed and that it will control the intraocular tension in some eyes in which other miotics are not effective. DFP also lowers the intraocular pressure in some eyes in which the glaucoma has not been controlled by surgical procedures.

Although, for these reasons, DFP is a valuable addition to the medical armamentarium against glaucoma, the drug does not fulfil all the requirements of an ideal antiglaucomatous miotic agent. It has several disadvantages. It frequently produces ciliary spasm, which has such undesirable effects as blurring, headache and brow ache. On rare occasions, an increase in tension may result from its use. This occurred in 6 eyes of the present series. This effect may be due to narrowing of the angle by an engorged ciliary body. DFP has been shown to dilate the ocular vessels and to increase the permeability of the smaller ones.[10] The increase in permeability may produce engorgement of the ciliary body and increase the protein content of the aqueous sufficiently to embarrass the angle. This mechanism should result in an increased intraocular tension more frequently in eyes with narrow angles than in those with wide angles. One cannot draw any definite conclusion from the results in 6 eyes. However, in 4 eyes gonioscopic examination showed narrow angles, whereas the other 2 eyes had wide angles, free of synechias. Haas [6] and Dunphy [7] suggested that eyes of the narrow angle type may be more prone to this increase in intraocular tension. It may be that the use of a vasoconstrictor agent, as suggested by the clinical studies of Sugar,[11] or of an antihistamine drug, as tried experimentally by von Sallmann,[10c] would prevent this rise in tension. The present data are insufficient to explain why, on rare occasions, an eye with narrow angle glaucoma showed a rise in tension, whereas in many other eyes with narrow angles the tension was controlled.

Ten eyes of 6 patients acquired sensitivity to DFP in peanut oil. In 4 patients this was shown to be a sensitivity to peanut oil, and in

10. (*a*) Leopold and Comroe.[1b] (*b*) Scholz, R.: Studies on the Ocular Reactions of Rabbits to Di-Isopropyl Fluorophosphate, J. Pharmacol. & Exper. Therap. **88**:23, 1946. (*c*) von Sallmann, L., and Dillon, B.: Effect of DFP on Rabbit Eyes, Am. J. Ophth. **30**:1244, 1947. (*d*) Aldrege, W. H.; Davson, H.; Dunphy, E. B., and Uhde, G. I.: Effect of DFP Vapor on the Eye, ibid. **30**:1405, 1947.

11. Sugar, S. H.: Acute Glaucoma, Am. J. Ophth. **30**:451, 1947.

2 patients, to DFP itself. Cessation of therapy resulted in rapid clearing of the local dermatitis. Preparations in liquid petrolatum may be used safely in some eyes sensitive to peanut oil.

Marr [9] reported a case of retinal detachment in a patient with high myopia following the use of DFP. No retinal detachment occurred in this series of 370 eyes, but we learned of a case in which the detached retina may have been due to DFP.[12] Macrae [12] saw a man aged 40 with a fairly high degree of myopia and chronic simple glaucoma in whom retinal detachment developed while he was under treatment with a 0.2 per cent solution of DFP. The retinal detachment was first noticed sixteen days after the beginning of daily DFP therapy. It is possible that ciliary spasm might result in retinal detachment, particularly in eyes with degeneration of the peripheral retina or marked retinal thinning. Gradle and Snydacker [13] reported 3 cases of retinal detachment following the use of pilocarpine and physostigmine in 447 glaucomatous eyes. Retinal detachment, therefore, occurs in glaucomatous eyes under treatment with other miotics.

Certain recommendations for the use of DFP may be made from this study. One should be fully aware of its many disadvantages before employing the drug. It is effective in cases of mild, early chronic simple glaucoma in concentrations as low as 0.01 per cent, but best results are obtained with concentrations of 0.025 to 0.1 per cent in peanut oil. The weaker the concentration successfully employed, the fewer the undesirable symptoms.

The drug will be helpful in some eyes with chronic simple glaucoma not controlled by other miotics, and it can also be employed safely in eyes which respond to other miotics. Fewer instillations of DFP will be required than of other miotics, and the diurnal fluctuations in tension will be reduced because of the greater length of action of DFP.

In cases of aphakic glaucoma, DFP appears to be the drug of choice, provided the glaucoma is not due to the vitreous block, described by Chandler and Johnson.[14] It is interesting to note how few aphakic patients are troubled by ciliary spasm. An occasional aphakic eye on which an extracapsular extraction had been performed had some symptoms. This observation suggested that firm insertion of zonular fibers must be present for the pain of ciliary spasm to develop.[1b] Dunphy [7] also noted this absence of symptoms in aphakic eyes and suggested

12. Macrae, H. M.: Personal communication to the authors.

13. Gradle, H. S., and Snydacker, D.: Retinal Detachment Occurring in Primary Compensated Glaucoma, Am. J. Ophth. **23**:52, 1940.

14. Chandler, P. A., and Johnson, C. C.: A Neglected Cause of Secondary Glaucoma in Eyes in Which the Lens Is Absent or Subluxated, Arch. Ophth. **37**:740 (June) 1947.

that it was due to the high cholinesterase content of the exposed vitreous body.

DFP can be used successfully in eyes with acute glaucoma in 0.05, 0.1 or 0.2 per cent concentration.

It is necessary to call attention to the strange relation of DFP and physostigmine. If physostigmine is instilled into a normal eye of a subject and fifteen minutes later, when the miosis has occurred, DFP is instilled in both eyes, the two pupils do not remain constricted for the same length of time. The eye that received DFP alone remains constricted for ten to fourteen days, whereas the eye that received both physostigmine and DFP returns to the preinstillation size in two to three days. In other words, physostigmine prevents the action of DFP. Physostigmine has protected the cholinesterase from the DFP.[15] This phenomenon has been demonstrated also in cats, in which a small dose of physostigmine protects against a subsequent large fatal dose of DFP.[3b] When the order of injection is reversed, the animals exhibit an increased and long-lasting sensitivity to physostigmine. These studies suggest that best results will be obtained with DFP when it has not been preceded by physostigmine or neostigmine, for these drugs will block the action of DFP against cholinesterase. However, if DFP is used first and physostigmine subsequently, the anticholinesterase effect will be enhanced. In other words, DFP should be used prior to physostigmine, and not in the reverse order.

SUMMARY

Di-isopropyl fluorophosphate (DFP) successfully lowered intraocular tension in 208 of 380 glaucomatous eyes.

DFP was effective in concentrations ranging from 0.01 to 0.1 per cent. The majority of eyes were controlled by a 0.05 to 0.1 per cent concentration of DFP in peanut oil.

Preparations of DFP in peanut oil were more effective than similar concentrations in liquid petrolatum U.S.P.

DFP lowered intraocular tension successfully in eyes with chronic glaucoma, acute glaucoma, buphthalmos, aphakic klaucoma and glaucoma secondary to uveitis and exfoliating lens capsule, although other miotics had previously failed. The best results were seen in eyes with aphakic glaucoma.

Decidedly fewer instillations of DFP were required to maintain a satisfactory intraocular tension in eyes in which the tension was also controlled by other miotics.

15. Comroe, J. H., Jr.; Todd, J.; Leopold, I. H.; Koelle, G. B.; Bodansky, O., and Gilman, A.: The Effect of Di-Isopropyl Fluorophosphate (DFP) upon Patients with Myasthenia Gravis, Am. J. M. Sc. **212**:641, 1946.

A fourteen month old solution of DFP in peanut oil showed no loss of potency.

DFP has several disadvantages when used as an antiglaucomatous miotic. It produces ciliary spasm, with associated brow ache, headache, eye ache and visual blurring. In 6 eyes in this series a rise in intraocular tension followed its local instillation. Local sensitivity may result from it or its solvent. Some patients acquire a resistance to its tension-lowering property after several months of treatment. Retinal detachments have been reported to follow its use in patients with high myopia.

Its action is inhibited by the previous use of physostigmine.

1930 Chestnut Street.

255 South Seventeenth Street.

ABSTRACT OF DISCUSSION

Dr. Leo L. Mayer, St. Louis: One of the difficulties Dr. Leopold mentions is the painful ciliary spasm. This can be overcome by using the lower concentration on the first administration of the drug. Then, gradually, the concentration of the drug can be increased as is seen fit; when the control period of the tension is below 30 mm. and no changes in the field occur, that concentration may be used thereafter.

With another type, absolute glaucoma, my experience has differed from the authors.[1] In the cases of absolute glaucomas which I have had to deal with, the principal reason for use of the miotic, and of DFP, was the intense pain. I admit that even when I used DFP the tension did not come down to normal, but in over 30 cases in which absolute glaucoma was present in one eye or in both eyes the patient was much more comfortable when the DFP was used than with other miotics, such as pilocarpine and physostigmine, and there was no pain whatever. I urge you to use DFP after operation for absolute glaucoma. Perhaps the patient has chosen not to have an operation; vision is gone, but he still complains of pain. With such patients, I feel, DFP has an additional use in relieving the pain, although it does not reduce the tension.

William F. Hughes Jr., Chicago: Dr. Leopold and Dr. McDonald have done a valuable service in presenting this follow-up study of their large series of patients with glaucoma treated with DFP. This confirmatory evidence of their previous study affords some reassurance to those of us who are occasionally disconcerted by the unfavorable responses of some patients. Their most striking results with DFP after other miotics had failed were obtained in the treatment of chronic narrow angle glaucoma, of secondary glaucoma complicating aphakia and following uveitis.

In order to compare the results obtained in the glaucoma clinic of the Illinois Eye and Ear Infirmary with those of Leopold and McDonald, the cases previously discussed in a preliminary report by Dr. Joseph Haas [6] before the Chicago Ophthalmological Society in December 1946, and several additional cases, are reviewed. The data have been classified in a manner identical with that used by Leopold and McDonald. A total of 40 eyes were given sufficient trial with DFP that its efficacy

could be determined. The tension of only 2 eyes had previously been controlled by other miotics, usually carbachol U.S.P. (carbamylcholine chloride) or, less frequently, a combination of pilocarpine and physostigmine. The average visual field efficiency was 25 degrees. The majority of the patients received 0.05 per cent DFP in peanut oil, usually as often as two or three times a day, if necessary, before its use was discontinued. In a few patients, the strength was increased to 0.1 per cent, without additional benefit. Of 18 eyes with chronic wide angle glaucoma, only 1 maintained normal tension and visual fields for four months under treatment with DFP. This patient had had one previous unsuccessful filtering operation and had received carbachol U.S.P., in addition to DFP. For 2 eyes in which the tension was previously controlled with carbachol the treatment was changed to DFP, and the tension remained normal for only three months. Of 4 eyes with chronic narrow angle glaucoma, 1 was controlled with DFP for four months. Of 10 aphakic eyes with glaucoma, 2 eyes (of the same patient) were controlled for twenty months with DFP. The drug failed to control the tension in 4 eyes with exfoliation of the lens capsule (open angle type), in 2 eyes with absolute glaucoma and in 2 eyes with juvenile glaucoma. In 17 of the eyes described previously, DFP did not produce any reduction of tension, even temporarily.

It is difficult to determine the reason for the discouraging results obtained in this small series of cases, in which only 1 of 13 eyes responded to DFP, as compared with the proportion of 1 of 2.4 eyes in the Leopold and McDonald series. Besides the great discrepancy in the total number of patients treated, the following differences in the two series may be of importance: 1. Many of the Chicago series had far advanced glaucoma, and the average visual field was only 25 degrees. Did the authors' patients who failed to respond to other miotics have such changes in the field? 2. Carbachol was used most frequently prior to the institution of DFP therapy, and this miotic was not used in the Philadelphia series. 3. A concentration of 0.1 per cent DFP was tried only infrequently in the Chicago series when instillations of 0.05 per cent two or three times a day failed to control the tension.

Leopold and McDonald's observation that D F P reduced the need for miotics in 10 eyes is interesting and the effect might well be due to the breaking of peripheral anterior synechias, as they suggest. This important effect of opening the drainage angle by means of the production of intense miosis may also explain the exceptionally good results which were obtained in their cases of narrow angle glaucoma, acute glaucoma and secondary glaucoma. In these cases, in which the angles were probably blocked, DFP produced good results in 64 per cent of 98 cases in which other miotics were ineffective, as compared with the normalization of tension in 33 per cent of 161 cases of wide angle glaucoma. This factor of angle block may represent an important indication for the use of DFP. However, this consideration must be weighed against the possibility of aggravating an existent embarrassment of the angle by the engorgement of the ciliary body, a highly protein aqueous and a shallow anterior chamber, such as followed the use of DFP in 6 eyes in the authors' series. This occurred in 3 eyes in the series I am reporting, not included in the 40 eyes in the previous series. In both

eyes of 1 patient with shallow angle glaucoma, the anterior chamber was completely absent; the eyes became excruciatingly painful, although not congested externally, and the tension rose from 35 to 80 mm. (Schiøtz) after the use of 1 drop of 0.05 per cent DFP twice a day for two days. Pilocarpine and phenylephrine hydrochloride (neosynephrine[R]) were then given locally and 50 per cent sorbitol was administered intravenously, the tension dropping to a range of 23 to 57 mm. Iridencleisis was then performed on each eye, after which the anterior chambers did not reform for two weeks. However, the tension has since remained normal, for a follow-up period of two months.

Six patients, not included in the series of the 40 eyes reviewed previously, refused to use DFP because of the symptoms it produced. Two complained of poor vision due to ciliary spasm; 2 had ocular pain, and 2, folliculosis of the conjunctiva due to hypersensitivity. None of the aphakic patients complained of discomfort.

The results in our cases have been poor, being at best only a temporary reduction of tension after other miotics had failed. In cases in which operation cannot be performed or must be deferred, DFP may be helpful. Although the infrequent need of instillation is an advantage, other miotics produce less objectionable symptoms, particularly in younger persons with good vision. DFP appears to be less effective in control of wide angle glaucoma, and it should be used in eyes with narrow angle glaucoma with caution because of the danger of immediate further embarrassment of the angle. However, DFP may be the miotic of choice in cases of aphakic glaucoma, in which it is well tolerated, or perhaps in treatment of any glaucoma in which powerful miosis is desired to open the filtration angle.

DR. RALPH RYCHENER, Memphis, Tenn.: During the past year DFP has been available to me in a limited amount, and I have had the opportunity to treat a total of 33 patients with various types of glaucoma. My results with primary glaucoma are very similar to those reported in the excellent paper by Leopold and McDonald.

In my series, I have had 3 cases of congenital glaucoma in which operation was unsatisfactory, or as yet inadvisable, and in which DFP was the only miotic which proved effective in maintaining normal intraocular pressure.

DR. ADOLPH POSNER, New York: In a series of cases of chronic simple glaucoma, I observed a number of instances in which a previously asymptomatic course was changed by the use of miotics. They were all cases of long-standing glaucoma, as evidenced by loss of field and deep cupping. The glaucoma was discovered accidentally, during routine examination. Prior to the institution of miotic therapy (usually pilocarpine) there were no subjective symptoms. Within a few months of treatment minor or major acute attacks began to develop. This indicates that DFP is not unique in producing acute attacks; miotics in general may alter the course of chronic simple glaucoma.

DR. EVERETT L. GOAR, Houston, Texas: During the past year I have been fortunate in having had available a supply of DFP, but the drug is extremely difficult to obtain unless one is connected with a medical school. Do the authors know when this preparation will be placed on the market, so that any ophthalmologist may obtain it? Several

professional colleagues in my section have borrowed from me and have not been able to pay it back. The drug has proved its usefulness and should now be made commercially available. DFP is not the answer to prayer for a cure for glaucoma, as it will accomplish only what a powerful miotic can, but it has proved its worth as an agent in the fight against glaucoma.

DR. P. ROBB MCDONALD, Philadelphia: Dr. Leopold and I are both aware that there is considerable variation in the reported results with the use of DFP. When the drug was first available, like Dr. Goar, we received many requests for its use and had probably as many unfavorable as favorable replies at that time. Most ophthalmologists were looking for the wonder drug that would reduce intraocular tension. The drug was, of course, used in those cases in which everything else had failed.

Our own patients were selected from the clinics of the University of Pennsylvania Hospital and Wills Hospital and were followed by us personally. A few patients were referred to us as having uncontrolled tension, which undoubtedly would have been controlled if there had been a change in their treatment; that is, we should not have needed to resort to DFP.

Our results are considerably more promising than those of Dr. Hughes, but I think he has stated the reasons himself. Though we did not mention it in our paper, we found that the DFP is less effective in cases of advanced than of early glaucoma. In some cases of glaucoma in which the field was greatly restricted, DFP might temporarily control the tension, but a tolerance to the drug was soon evident.

We have not used carbachol to any extent in Philadelphia. We have used 20 per cent methacholine chloride (mecholyl [R]) in conjunction with DFP, with good effect in some cases. We have also used epinephrine bitartrate and phenylephrine in conjunction with DFP. These drugs counteract the vasodilator effect of DFP.

DFP may be an heuristic drug, as well as of some value in the treatment of glaucoma. Several interesting observations have been made. In the normal eyes its action is much longer than in the glaucomatous eye. This confirms the observation that there is a disturbance in the acetylcholine-cholinesterase balance in a glaucomatous eye. Little is known about the effect of DFP on the aqueous barrier. It may be that the primary action is there, rather than on the angle.

We believe that DFP is of value in the treatment of glaucoma. It is a drug which should be used with discretion. Both the physician and the patient should be aware of what might happen. If the tension is checked two or three hours after the first administration, acute glaucoma can probably be avoided and, if used judiciously, the drug may prove of some value.

As to Dr. Goar's inquiry when DFP will be available, all we can say is that the drug is at present under consideration by the Food and Drug Administration and that if they pass it it will be available throughout the country. The paper which we have read today may have some effect in expediting its release.

LATTICE TYPE OF HEREDITARY CORNEAL DEGENERATION

Report of Five Cases, Including One of a Child of Two Years

FREDERICK C. STANSBURY, M.D.
SYRACUSE, N. Y.

THE LATTICE type of familial corneal dystrophy was first described in 1890 by Hugo Biber,[1] a pupil of Haab, as *gitterige Keratitis*. He called it a chronic disease of the cornea, producing a bilateral opacity which at first looked like the residue of interstitial keratitis. The margin of the cornea was spared. Close examination revealed that the opacity was due to a lattice-like system of lines and to fine, rounded dots, which together resembled a spider's web. In regard to the lines, Biber said:

> They run in various directions and sometimes cross each other. They remind one of a birch twig, branching here and there. Ledgelike projections on the surface of the cornea appear to correspond to these lines.[1]

Symptoms of inflammation were insignificant, and at most included slight congestion and photophobia. The disease ran a long and painless course, eventually resulting in serious impairment of vision. Biber described this condition in 3 unrelated adults, aged 39, 52 and 62 years, respectively.

Haab,[2] who is usually credited with first describing *gitterige Keratitis*, published a follow-up observation on Biber's cases in 1899 and included 3 new ones of his own. In Biber's cases there was a marked decrease in corneal sensitivity at that time; the periphery of the corneas was still clear, and there was no vascularization. Haab's first cases were those of a boy of 16 years and his maternal aunt and uncle. The first complaint of these patients was blurred vision; there was little or no irritation of the eyes. Haab found that the corneas were rough superficially, showed no blood vessels but exhibited a latticework of gray lines and dots. He stated:

> The lines show in general a radial arrangement, especially the longer ones. Moreover, they are often forked, the work being open toward the center of the

From the Institute of Ophthalmology of the Presbyterian Hospital of the City of New York.

1. Biber, H.: Ueber einige seltenere Hornhauterkrankungen (Ulcus rodens, Keratomalacie Neugeborener, recidivierevale Keratitis bullosa nach Trauma, gitterige Keratitis), Inaug. Dissert., Zurich, A. Diggelmann, 1890, pp. 35-42.

2. Haab, O.: Die gitterige Keratitis, Ztschr. f. Augenh. **2**:235-246, 1899.

cornea. Still, one sees here and there a fork that is open toward the periphery. Some of the lines bend after running toward the center of the cornea, forming the arc of a large circle. The lines throughout have a somewhat undulating course, and their arrangement reminds one of twigs or the figures which one sees on a frosted window. Between the lines one sees small gray spots and points. The figures are transparent and light reflecting, so that the spots look like drops of water and the lines resemble threads of crystal.[2]

Pathologically, Haab noted a transparent substance deposited in and below Bowman's membrane. It was still present after the epithelium was scraped off and was considered to be a hyaline degenerative process. Haab rejected the idea that the lines were connected in any way with the distribution of the nerve fibers, nor did he believe that they were fine vessels left by a preceding interstitial keratitis. It was he who first called attention to the familial nature of the lesion.

In the same year that Haab's paper appeared (in fact, in the same volume of the *Zeitschrift für Augenheilkunde*), Dimmer [3] published a report of 3 siblings afflicted with the lattice-like corneal opacities. Their ages ranged from 47 to 57 years, and they had had the disease for twenty to thirty years. Dimmer found that all 3 patients had had recurrent inflammatory attacks during their youth, and he attributed this condition to rubbing of the inner part of the lid on the cornea. Pathologically, he described many punctiform hyaline and crystalline masses in the substantia propria and in Bowman's membrane. Examination of particles of these corneas revealed a colloidal or hyaline substance and triple phosphates. Dimmer's clinical description of his 3 cases was similar to those of Biber and Haab. He called attention to the fact that the lines were best seen by reflected light.

Soon after the publication of the cases of Haab and Dimmer, other reports of lattice-like degeneration of the cornea began to appear in the literature. In 1901, Hauenschild[4] reported a typical case. In 1902, Treacher Collins [5] described a typical case of reticular degeneration, although he gave it no name. Casper[6] described a case in 1903, calling the condition a lattice-like corneal opacity and ascribing it to trauma. In the same year, Freund[7] reported 15 cases, 7 in one family and 8

3. Dimmer, F.: Ueber oberflachliche gittrige Hornhauttrübung, Ztschr. f. Augenh. **2**:353-361, 1899.

4. Hauenschild, W.: Ein Fall von gittriger Keratitis, Ztschr. f. Augenh. **6**:139-141, 1901.

5. Collins, T.: A Case Presenting an Unusual Form of Opacity in the Central Part of Each Cornea, Tr. Ophth. Soc. U. Kingdom **22**:148-150, 1902.

6. Caspar, L.: Gitterförmige Hornhauttrübung nach Augenverletzungen, Klin Monatsbl. f. Augenh. **41**:289-293, 1903.

7. Freund, H.: Die gittrige Hornhauttrübung, Arch. f. Ophth. **57**:377-399, 1903.

in another, covering four generations in each family. In 1904, Fehr[8] reported a case, and Spicer[9] described the condition in a father and his daughter and called it nodular degeneration, even though he suggested that the term "reticular" was more appropriate. In 1907, Patterson[10] reported a typical case under the title "reticular opacity of the cornea." In 1908, Kipp[11] recorded the first case in the American literature. In 1909, Jacqueau,[12] in France, described 8 cases occurring in three generations of the same family.

DIFFERENTIATION FROM GROENOUW'S NODULAR DEGENERATION

The elucidation of lattice-like dystrophy of the cornea is complicated by the fact that Groenouw[13] described another, very similar, form of hereditary corneal degeneration at the same time (1890) that Biber published his report. Groenouw first discussed 2 cases of the lesion he called *knötchenformige Hornhauttrübungen,* in a man aged 50 and in an unrelated woman aged 20. He stated:

> The disease consists in the development of numerous small, rounded or irregular, gray, discrete opacities in the otherwise clear corneal tissue. The larger opacities attain a diameter of about 0.25 mm., and between them lie many smaller, dustlike, gray points. The spots are situated chiefly in the central region of the cornea and leave the margin free for the most part. The larger nodules raise the epithelium somewhat and thus give an irregular curve to the corneal surface. The opacities appear to form gradually, without inflammatory reaction, and they remain unchanged for years.[13]

Eight years later, Groenouw[14] reported on a histologic study of a small piece of cornea excised in one of these cases. He noted a foreign material deposited in discrete patches in the superficial layers of the corneal stroma, sometimes just beneath the epithelium but never within it. With hematoxylin and eosin, this material took an acidophilic stain, and he suggested a probable hyaline nature. The nuclei of the corneal

8. Fehr, I.: Ein Fall von gittriger Hornhauttrübung, Centralbl. f. Augenh. **28**:173-176, 1904.

9. Spicer, W. T. H.: Nodular Opacities of the Cornea in Father and Daughter, with a History of the Same in the Father's Brother and Sister, Tr. Ophth. Soc. U. Kingdom **24**:42-45, 1904.

10. Patterson, J. V.: A Case of Reticular Opacity of the Cornea (gittrige Keratitis, Haab), Ophth. Rev. **26**:223-226, 1907.

11. Kipp, C.: A Case of Grill-Like Keratitis, Tr. Am. Ophth. Soc. **11**:537-540, 1908.

12. Jacqueau, L.: Une forme de kératite héréditaire et familiale, Clin. opht. **15**:434-439, 1909; abstracted, Jahresb. u. Ophth., 1909, p. 649.

13. Groenouw, A.: Knötchenformige Hornhauttrübungen, Arch. f. Augenh. **21**:281-289, 1890; translated, Arch. Ophth. **19**:245-254, 1890.

14. Groenouw, A.: Knötchenförmige Hornhauttrübungen, Arch. f. Ophth. **46**: 85-102, 1898.

cells were slightly increased in the vicinity of these deposits. He observed no significant changes in the epithelium; Bowman's membrane was largely missing, and there were no signs of inflammation. In 1917, Groenouw[15] reported a series of cases in three generations of this family, adding only that the process was slowly progressive, with new foci continually forming, and that the opacities increased in size by fusing with other opacities. Finally, in 1933, he[16] published a paper describing his observations on this process in four generations of the same family.

It was inevitable that some one should postulate that such similar corneal lesions are manifestations of the same underlying process. Fleischer[17] did so in 1905, in a paper in which he grouped the nodular type of Groenouw and the lattice type of Biber, Haab and Dimmer together as forms of familial corneal degeneration, the lesions varying in different cases but actually having many characteristics in common. He expressed the belief that the same etiologic factors are present in the two types. He added that the nodular type is inclined, in the course of years, to be transformed into the reticular type by the fusion of many foci. He added a new variation, the ring-shaped type, in which the opacities take the form of rings, or partial rings. This form, he stated, may be found alone, or in the same cornea with the nodular or the reticular type.

Support was soon furnished Fleischer's stand by the reported observation of the different types of opacities in the same person and, even more frequently, in the same genealogic tree. Doyne and Stephenson,[18] in 1905, reported 5 cases of a combined nodular and reticular type in one family. Folker[19] described 9 cases in three generations of a family; 7 were of the nodular type and 2 of the reticular type. Roy[20] reported 6 cases in the same family, in 1 of which the lattice-like configuration appeared. Weeks[21] described 2 cases of combined lattice and nodular keratitis in father and son. Neame[22] reported a case of

15. Groenouw, A.: Knötchenförmige Hornhauttrübungen, vererbt durch drei Generationen, Klin. Monatsbl. f. Augenh. **58**:411-420, 1917.

16. Groenouw, A.: Knötchenförmige Hornhauttrübungen, vererbt durch vier Generationen, Klin. Monatsbl. f. Augenh. **90**:577-592, 1933.

17. Fleischer, B.: Ueber familiäre Hornhautentartung, Arch. f. Ophth. **53**:263-344, 1905.

18. Doyne, R. W., and Stephenson, S.: Upon Five Cases of Family Degeneration of the Cornea, Ophthalmologica **3**:213-221, 1905.

19. Folker, H.: Nodular Opacity of the Cornea in Three Generations, Tr. Ophth. Soc. U. Kingdom **23**:42-52, 1909.

20. Roy, D.: Report of Six Cases of Degeneration of the Cornea in the Same Family (Nodular Keratitis), Tr. Am. Ophth. Soc. **13** (pt. 1):101-108, 1912.

21. Weeks, J.: Family Nodular Keratitis, Arch. Ophth. **42**:179-180, 1913.

22. Neame, H., in discussion on Hine,[23] p. 45.

familial degeneration, with the reticular form in the right eye and the nodular form in the left eye. Hine,[23] describing the disease in a mother and her two children, said that the mother and son exhibited the nodular form, with some rings scattered among the lesions, and the daughter a pure lattice type. Gutzeit [24] also reported both nodular and reticular forms in the same family. Ladekarl,[25] combining all forms into one clinical entity, suggested that when the subepithelial deposits predominate the nodular form results, but that when most of the changes are in the superficial layers of the substantia propria the reticular form is more likely to be present. Srivinasan[26] reported on an interesting family with 7 cases of familial corneal dystrophy, all in female members. Three were cases of the lattice type; 2, of Groenouw's nodular form, and 2, early cases of an undetermined type. Judd,[27] in this country, reported 9 cases occurring in three generations of a family; both nodular and reticular forms were present. He also stated the belief that the two types were manifestations of the same process.

In 1935, Frykholm [28] published an extensive investigation of six generations of an afflicted family, the most complete genealogic study of the disease in the literature to date. In all, he found 42 cases of familial corneal dystrophy, involving 21 male and 21 female members. He described the clinical findings in 13 persons of the last three generations. In general, the younger persons showed the lattice-like opacities, while the older ones had the nodular type. He presented this observation as additional information that the two types are related. Freiberger[29] reported 11 cases, all of the nodular type except that of the youngest child, whose cornea showed some vertical streaks. Somerset[30] discussed 3 cases of a condition he called mixed corneal dystrophy, showing lines, nodules and ring forms.

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23. Hine, M. L.: Familial Nodular and Reticular Keratitis, Proc. Roy. Soc. Med. (Sect. Ophth.) **16**:43-45, 1923.

24. Gutzeit, R.: Ueber familiäre knötchenförmige Hornhauttrübung, Ztschr. f. Augenh. **68**:349-353, 1929.

25. Ladekarl, P. M.: Two Atypical Cases of Keratitis Nodosa Groenouw, with Histological Examinations, Acta ophth. **8**:213-232, 1930.

26. Srivinasan, E. V.: A Family of Groenouw's Dystrophy, Brit. J. Ophth. **16**:296-297, 1933.

27. Judd, J. H.: Nodular Degeneration of the Cornea, Am. J. Ophth. **16**:310-318, 1933.

28. Frykholm, R.: Familiäre Hornhautentartung, vererbt durch sechs Generationen: Klinisch nachgewiesen bei dreizehn Mitglieden der dreizehn Letzen, Klin. Monatsbl. f. Augenh. **94**:76-106, 1935.

29. Freiberger, M.: Corneal Dystrophy in Three Generations, Arch. Ophth. **16**:257-270 (Aug.) 1936.

30. Somerset, E. J.: Three Cases of Corneal Dystrophy, Proc. Roy. Soc. Med. **30**:389-394, 1937.

CLASSIFICATION

Bücklers,[31] in 1938, published the results of an extensive survey undertaken for the German government under the program for the sterilization of the unfit. He claimed that his study proved genetically and clinically that there are three distinct types of hereditary corneal dystrophy. A total of 129 affected persons from about 600 families were examined. Ninety-one cases were of the granular type; 32, of the spotty type, and 6, of the lattice-like form. Bückler's classification of the hereditary corneal dystrophies is as follows:

Nodular (or granular) type (Groenouw I)	Dominant
Spotty (or macular) type (Groenouw II, Fuchs, Fehr and Fleischer	Recessive
Grill-like type (Haab, Dimmer)	Dominant

According to Bücklers, all types begin in the first decade of life, but only the spotty form attracts attention at an early age, because of its serious effect on the visual acuity. The other two types may continue for years before the painful attacks of the lattice form, and the failing vision of the granular form, attract attention. Vascularization does not occur in any of the three forms. Ulcers of the epithelium were noted only in the lattice form, but pain and lacrimation also occurred in the macular form. Bücklers found consanguinity in all the 7 pedigrees which he investigated. However, the blood relationship was obscure in some of the pedigrees and had to be traced back eight to eleven generations. He stated that it is impossible to find combined forms and that, genetically, each type is transmitted in pure form. He also stated that only the type with double-contoured lines, with clear intervals between them, should be considered a true reticular corneal dystrophy.

Berliner,[32] in this country, adopted Bückler's classification and stated that under optical section the lines appear as optically empty tubes, and may be linear, fusiform, oval or round. Franceschetti and Babel[33] recently (1945) published a classification of hereditary and congenital corneal dystrophies, in which they adopted Bückler's system of division for the hereditary types. Von der Heydt,[34] discussing the types of corneal dystrophies, also endorsed Bückler's classification.

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31. Bücklers, M.: Die erblichen Hornhautdystrophien, Klin. Monatsbl. f. Augenh. **99**:676-681, 1937; The Three Forms of Familial Corneal Degeneration and Their Hereditary Transmission, Arch. Ophth. **18**:331-332 (Aug.) 1937.

32. Berliner, M. L.: Biomicroscopy of the Eye, New York, Paul B. Hoeber, Inc., 1943, vol. 1, pp. 324-339.

33. Franceschetti, A., and Babel, J.: Essai de classification anatomique des dégénérescences familiales de la cornée, Ophthalmologica **109**:169-202, 1945.

34. von der Heydt, R.: Corneal Dystrophies: Types, Am. J. Ophth. **20**:738-740, 1937.

Mutch,[35] in England, published (1944) a comprehensive review of hereditary corneal dystrophies and discussed 24 cases of the granular type. He listed the following nine characteristics that the three types have in common:

1. The disease is bilateral and reasonably symmetric.
2. Onset is in the first decade of life.
3. Nodules are present, causing irregularity of the corneal surface.
4. Vascularization is absent.
5. Attacks of pain are common.
6. The central portion of the cornea is affected first, and in the dominant forms the periphery is not involved.
7. The etiologic agent is unknown.
8. The disease is resistant to any form of medical treatment.
9. It is not associated with any other known disease or defect.

Mutch also discussed the differential diagnosis of the three types, and tabulated the main points of differentiation, as follows:

Chief Differences	Granular Type	Reticular Type	Macular Type
Shape of opacities.....	Irregular, discrete granules	Interlacing lines and nodules	Spots so numerous as to form a diffuse opacity
Situation of opacities...	Axial region	Axial region	Whole cornea, denser in the axial region
Vision.....	Good until middle age	Affected early	Affected early
Hereditary transmission	Dominant	Dominant	Recessive
Corneal sensation.....	Good	Defective	Defective

No attempt is made in this paper to present the whole subject of the hereditary corneal dystrophies. The nodular form is much commoner than the lattice-like type, and many reports of the former appear in the literature. Only papers pertaining to both the nodular and the reticular form have been discussed here, in an effort to determine whether the reticular form is an entity or merely a subdivision or deviation of the commoner, nodular, type. It would seem that clinically, at any rate, the weight of opinion favors lattice dystrophy as an entity.

Additional reports on the incidence of the pure reticular form have been published as follows: Goulden,[36] 1 case; Zaun,[37] 1 case; Adrogué,[38] 1 case; Jeandelize and Bretagne,[39] 1 case; Koby,[40] 1 case; Caddy,[41] 1

35. Mutch, J. R.: Hereditary Corneal Dystrophy, Brit. J. Ophth. **28**:49-86, 1944.

36. Goulden, C.: Reticular Opacity of the Cornea, Tr. Ophth. Soc. U. Kingdom **41**:193-194, 1921.

37. Zaun, W.: Ueber die gitterige Hornhauttrübung, Klin. Monatsbl. f. Augenh. **72**:151-154, 1924.

38. Adrogué, E.: Lattice-Like Degeneration of the Cornea, Rev. Soc. argent. de oftal. **1**:32-39, 1925; Semana méd. **32** (pt. 2):1657-1659, 1925.

39. Jeandelize, P., and Bretagne, P.: Un cas de kératite héréditaire et familiale vu en microscopie oculaire, Ann. d'ocul. **163**:608-613, 1926.

(Footnotes continued on next page)

case; Löwenstein,[42] 2 cases; Greenwood,[43] 5 cases; Nemeth,[44] 3 cases; Shapira,[45] 3 cases; von der Heydt and Gradle,[46] 1 case; Aurand,[47] 3 cases; Maury,[48] 1 case; Hruby,[49] 1 case; Lloyd,[50] 4 cases; Hesse,[51] 8 cases; Cavka,[52] 1 case; Streiff,[53] 1 case; Fuchs,[54] 8 cases; Byers,[55] 1 case; Pillat,[56] 1 case, and Hermann,[57] 7 cases. Altogether, 96 cases of definite lattice corneal dystrophy can be found in the literature up to the present. The 5 cases in this report make a total of 101 cases. The cases of mixed, or questionable, type that have already been noted as deviations from, or atypical forms of, Groenouw's dystrophy have not been included in this figure.

ETIOLOGY

Little, or nothing, is known concerning the etiology of this bizarre lesion of the cornea. Biber, Haab and Dimmer expressed no opinion as to the cause, except that it seemed to be a chronic degenerative process. Groenouw[13] suggested a nutritive disturbance on a hereditary basis to

40. Koby, F. E.: Sur la dégénérescence réticulaire superficielle de la cornée, Arch. d'opht. **44**:149-166, 1927.

41. Caddy, A.: Reticular Opacity of the Cornea, Proc. Roy. Soc. Med. (Sect. Ophth.) **21**:412 and 826, 1928.

42. Löwenstein, A.: Zur Klinik, Histologie und Therapie der gitterförmige Hornhautdegeneration, Klin. Monatsbl. f. Augenh. **82**:752-762, 1929.

43. Greenwood, A.: Lattice Keratitis: Studies of Four Cases Observed in One Family, Tr. Am. Acad. Ophth. **35**:248-258, 1930.

44. Nemeth, L.: Ueber die gitterige Entartung der Hornhaut, Klin. Monatsbl. f. Augenh. **95**:73-76, 1935.

45. Shapira, T. M.: Lattice Type of Corneal Dystrophy, Arch. Ophth. **14**: 387-391 (Sept.) 1935.

46. von der Heydt, R., and Gradle, H. S., cited by Shapira.[45]

47. Aurand, D.: Trois cas de kératite en grillage observes dans la même famille, Arch. d'opht. **52**:684-685, 1935.

48. Maury, F. H.: The Pathology of Lattice and Nodular Dystrophy of the Cornea, Am. J. Ophth. **19**:866-872, 1936.

49. Hruby, K.: Gitterige Hornhautdystrophie, Klin. Monatsbl. f. Augenh. **103**:342-343, 1939.

50. Lloyd, R.: A Family with Lattice Dystrophy of the Cornea, Tr. Am. Ophth. Soc. **37**:120-126, 1939.

51. Hesse, E.: Beitrag zum Beginn und sur Erblichkeit der gittrigen Hornhautdystrophie, Arch. f. Ophth. **141**:1-19, 1940.

52. Cavka, V.: Beitrag zur familiären Hornhautdegeneration, Klin. Monatsbl. f. Augenh. **106**:348-352, 1941.

53. Streiff, E. B., cited by Franceschetti and Babel.[33]

54. Fuchs, E.: Ueber knöchenförmige Hornhauttrübung, Arch. f. Ophth. **53**: 423-438, 1901-1902; reviewed, Ophth. Rev. **21**:187-190, 1902.

55. Byers, W.: Reticular Keratitis, Am. J. Ophth. **3**:717-721, 1920.

56. Pillat, A.: Ueber gitterige und andere Formen degenerativer Hornhauterkrankungen, Klin. Monatsbl. f. Augenh. **69**:681-682, 1922.

57. Hermann, C.: La dystrophie grillage de la cornée, Ophthalmologia **112**: 350-363, 1946.

explain his nodular type. Fuchs,[54] discussing both types, mentioned a glandular disturbance merely as a possibility; he found an enlarged thyroid in 1 of his cases but no signs of hyperthyroidism. Wehrli,[58] writing primarily of Groenouw's type, observed tissue changes suggestive of tuberculous nodules and, in a single preparation, a few acid-fast bacilli, which he considered tubercle bacilli of low virulence. He therefore suggested a tuberculous basis for the disease, similar in character to lupus of the skin. Green[59] reported a case of severe tuberculous involvement of the skin, as well as nodular opacity of the cornea, and expressed agreement with Wehrli that the hereditary corneal dystrophies may be tuberculous. Schieck [60] stated that the tuberculosis was probably an associated condition. Fuchs[61] suggested primary hereditary degeneration of the connective tissue, allied in nature to arteriosclerosis. Byers[55] regarded the lines as "corrugations" of Bowman's membrane due to slight chronic hypotonicity and called the condition "anterior corrugation of the cornea."

Treacher Collins,[62] addressing the International Congress of Ophthalmology in 1922, included the familial corneal dystrophies with hereditary ocular degenerations (retinitis pigmentosa, macular pigmentary degeneration, amaurotic familial idiocy and Leber's [hereditary] optic atrophy), all of which he considered due to premature loss of vital force, or abiotrophy. He suggested that the corneal lesions are primary dystrophies of the corneal nerves and end organs, followed by thickening of the neuroglial tissue surrounding the nerves, hyaline degeneration and formation of spaces filled with coagulum, representing those previously filled with nerve tissue. If the nerve fibers are particularly involved, the lattice-like variety is the end result; if the end organs are primarily affected, the nodular form develops.

Pillat,[56] in agreement with Collins, stated that the primary causative factor is a degenerative process affecting the trigeminal nerve. In his

58. Wehrli, E.: Die knötchenförmige Hornhauttrübung Groenouw [18]) eine primäre isolierte, chronische, tuberkulose Erkrankung der norderen Schichten der Cornea: Lupus Cornea, Ztchr. f. Augenh. **13**:322-334, 1910; Weitere klinische und histologische Untersuchungen über den unter dem Bilde der knötchenförmige Hornhauttrübung (Groenouw [18]) verlaufenden chronischen Lupus der Hornhaut, Arch. f. Ophth. **55**:126-184, 1906.

59. Green, J.: Nodular Opacity of the Cornea, with Special Reference to Its Etiology, J. A. M. A. **53**:920-924 (Sept. 18) 1909.

60. Schieck, F.: Die Degenerationen der Cornea, in Schieck, F., and Bruckner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931, vol. 4, pp. 398-403.

61. Fuchs, A.: Zur Kenntnis der gitterigen Hornhautentartung: Haab-Dimmer, Ztschr. f. Augenh. **57**:159-186, 1925.

62. Collins, T.: Hereditary Ocular Degenerations: Ophthalmic Abiotrophies, Tr. Internat. Cong. Ophth. **1**:103-143, 1922.

case, he reported a reduction of sensibility over an area supplied by the ophthalmic and maxillary branches of the fifth nerve, as well as a highly reduced corneal sensitivity. He expressed agreement with Collins as to the mode of production of the two forms and explained the lesion as a primary neurotrophic disturbance, followed by secondary necrobiosis. According to Pillat, when the nerve fibers and the terminal plates are both involved, the mixed variety, or reticulonodular form, results. Gutzheit[24] also advocated Pillat's neurotrophic disturbance as the cause.

Kraupa,[63] working in the Elschnig clinic, also agreed with Collins that the primary cause was neurotrophic and claimed that the lesions were demonstrable changes resulting from degeneration of the corneal nerves. Koby,[64] in his book on biomicroscopy of the eye, stated that reticular keratitis is due to chronic inflammation of the corneal nerves. He also offered folds or ruptures in Bowman's membrane as an etiologic possibility. Löwenstein,[42] working in the Elschnig clinic but pursuing his investigations independently, came to the same conclusions as Collins, Pillat and Kraupa.

However, Stanka,[66] another member of the Elschnig staff, stated his disagreement with Kraupa and Löwenstein and claimed to have proved that the grillwork is not connected with the corneal nerves. According to Stanka, the central portion of the cornea is so extensively damaged that it could not possibly be secondary to a neural degeneration. If it were, the corneal sensitivity, he stated, should always be totally abolished, whereas it is usually only moderately reduced, or even normal. Moreover, Stanka said he could demonstrate by vital staining that there was never a direct contact between the nerves and the degenerative foci. By means of the slit lamp, he detected a decrease in the number of limbal capillaries and frequent aneurysms at the bifurcation of the limbal vessels. Stanka concluded that failing nutrition of the cornea, due to these anomalies, was the primary causative factor.

PATHOLOGIC FEATURES

Since the total number of cases of lattice dystrophy reported to date is small, and because few eyes so afflicted are likely to reach the pathologic laboratory, knowledge of the pathologic characteristics is meager.

63. Kraupa, E.: Die familiär degenerativen Hornhautveränderungen im System des sogenannten Dystrophien der Hornhaut, Klin. Monatsbl. f. Augenh. **70**:397-398, 1923.

64. Koby, F.: Slit Lamp Microscopy of the Living Eye, Philadelphia, P. Blakiston's Son & Co., 1925, p. 103.

65. Footnote deleted.

66. Stanka, R.: Ueber familiäre gitterige Hornhautdegeneration, Klin. Monatsbl. f. Augenh. **7**:357-360, 1925.

Haab and Dimmer reported discrete deposits of hyaline-like material in the anterior third of the stroma and in Bowman's membrane. Freund [7] observed the same deposits of hyalin and absence of Bowman's membrane.

Fuchs,[67] in 1915, published the results of his thorough study of the nodular form. He described two primary changes: (1) a subepithelial secretion of an acidophilic substance, and (2) a basophilic substance in the superficial layers of the corneal stroma. He also noted fissure formation, epithelial overgrowth, thinning and disturbances of Bowman's membrane and swelling and partial disappearance of the corneal lamellas. These two staining reactions were not confirmed until 1940, when Löwenstein [68] reported similar findings in 3 cases of nodular dystrophy: acidophilic material anterior to Bowman's membrane and basophilic masses in the anterior stroma. He emphasized that the distinction between the two substances was perceptible only in those places where Bowman's membrane was preserved.

Paderstein [69] stated that the nodular form of Groenouw is a primary degeneration of the epithelium: The nuclei are destroyed, and the protoplasm is changed into a hyaline substance, which tends to accumulate on the surface of Bowman's membrane. In his case, the pathologic changes were observed exclusively in the epithelium, anterior to Bowman's membrane, and the stroma was unaltered. Puscarin,[70] Uhthoff [71] and Wirth [72] also described epithelial changes similar to those of Paderstein. Fuchs [54] stated the opinion that the flattening of the epithelium above the nodules and the destruction of Bowman's membrane were purely mechanical changes caused by the pressure. Ladekarl [25] stated that the epithelial changes were too pronounced to be considered secondary changes due to mechanical pressure.

The first complete pathologic examination in a case of lattice dystrophy was that of Maury,[48] in 1936. His patient had had an optical iridectomy by another ophthalmologist, followed by extraction of a postoperative cataract. After the extraction, the eye became painful, shrunken and

67. Fuchs, E.: Ueber knötchenförmige Hornhauttrübungen, Arch. f. Ophth. **89**:336-349, 1915.

68. Löwenstein, A.: Glass Membranes in the Eye, Am. J. Ophth. **23**:1229-1242, 1940.

69. Paderstein, R.: Bemerkungen zu Wehrli's Kritik meines Falles von knotchenförmiger Hornhautdegeneration, Klin. Monatsbl. f. Augenh. **47**:156-167, 1909.

70. Puscarin, E.: Deux observations d'opacité nodulaires de la cornée (Maladie de Groenow), Arch. d'opht. **33**:362-373, 1913.

71. Uhthoff, W.: Weitere klinische und anatomische Beiträge zu den degenerativen Erkrankungen der Hornhaut, Klin. Monatsbl. .fAugenh. **55**:290-299, 1915.

72. Wirth, M.: Zur Histologie der knötchenförmigen Hornhauttrübung, Ztschr. f. Augenh. **58**:106-114, 1926.

blind, and enucleation was carried out. Immediately after the enucleation, the cornea was divided into numerous sections so that different portions could be subjected to different histologic technics. A study of one portion, with supravital staining with methylene blue, revealed that the lattice fibers were in no way connected with the corneal nerves. Another portion, subjected to the Bielschowsky silver stain, also revealed no relation between the nerves and the opacities, although both were well impregnated with silver. Frozen sections were stained with strong solution of iodine U. S. P., and a negative reaction for amyloid was obtained.

Frozen sections, both fixed and unfixed were stained with sudan III (C. I. No. 248) for fat. The nodular and lattice opacities had a homogeneous red appearance with this stain, and minute deposits, invisible with other stains, were readily seen in these sections. In the smallest lesions, the hyalin-lipid deposits could be clearly seen within the fibers of the corneal stroma. In the central zone of the cornea, Bowman's membrane stained with sudan III in several places.

With hematoxylin and eosin, the corneal opacities appeared as pink-staining, hyalin masses, sometimes homogeneous and sometimes laminated. With the Van Gieson stain, the masses took a light yellow tint. With Mallory's stain for connective tissue the deposits were colored orange, in sharp contrast to the blue-staining normal corneal lamellas. The best differentiation was obtained in a portion fixed in solution of mercury bichloride U. S. P.; the involved corneal corpuscles were scanty, and those that were seen appeared small and shrunken. The uninvolved corneal lamellas appeared normal. No hyalin deposits were seen in the epithelium. Maury concluded that the primary lesion was a deposition of hyaline material in the corneal corpuscles themselves.

Another good pathologic description of the lattice form is found in the paper of Franceschetti and Babel,[33] in which they described sections loaned to them by Prof. E. B. Streiff. They found the epithelium involved: thickened in some places, thin in others and flattened out completely in still other aspects. Bowman's membrane was destroyed for the most part. Where it was present, it was separated from the epithelium by a little connective tissue. In the anterior layers of the stroma, these authors noted thickened, hyalinized lamellas. There was a great abundance of deposits and granulations, of such variable shapes that the normal structure of the lamellas was destroyed. The smallest deposits were seen in the interior of the lamellas; the largest ones had destroyed the lamellas completely. Many of the deposits were subepithelial.

Franceschetti and Babel reported that all the granulations were strongly basophilic, that they were partially stained with gentian violet and that they stained brownish yellow with strong solutions of iodine U. S. P. Stained with hematoxylin and eosin, the pink-staining masses

were not homogeneous; the centers were darker. With the Masson trichrome stain, there was seen double staining: red and green. With the Van Gieson stain the masses were black, and with Mallory's stain, a deep red. They stated the belief that the hyalinized thickened lamellas seen throughout the parenchyma were probably the anatomic basis for the lattice fibers and that the basophilic masses were the nodules.

In 1946, Hermann [57] published an excellent clinical and pathologic description of 7 cases, all occurring in one family. Pathologically, the epithelium was observed to be very irregular, being thick in some places and very thin in others. The polyhedral and basal cells were completely gone; only flat, squamous-like cells were present. Bowman's membrane was not present; in its place, numerous amorphous masses were seen, causing "bumps" which pushed into the epithelium. Similar masses were seen in the anterior layers of the stroma. Many of the corneal fibers in these layers were swollen and degenerated; there were no signs of inflammation. With the trichrome stain, the masses were red; with the Van Gieson stain, yellowish, and with hematoxylin and eosin, pink. There was no trace of lipid deposits. The May-Greenwald-Giemsa stain revealed two types of masses: the first, red, were extremely small and were located inside the superficial lamellas of the cornea; the second, blue, were larger and variable in size and were observed subepithelially and between the corneal lamellas. Hermann found the optically empty tubes, as described by Bücklers, only in the early stages; later the tubes became filled with the hyalin material and were refractile.

TREATMENT

Diseases of unknown etiology and obscure pathology are usually difficult to treat, and that is certainly true of the familial dystrophies. Therapy in most cases has been merely palliative and expectant, although a great variety of medicaments have been tried, empirically. Iodides, preparations of mercury and tuberculin have been used systemically. As drops, zinc sulfate, boric acid, silver nitrate, potassium iodide, resorcinol and colchicum have been instilled. Iodoform, ethylmorphine hydrochloride, jequiritol and mild mercurous chloride U. S. P. have been used as dusting powders. Yellow mercuric oxide, ichthammol and boric acid have been prescribed in ointment form. Use of thyroid and ovarian extracts, vitamin A, liver and iron has been unsuccessful. Heat and cold have been tried by many. Some have attempted to increase the nourishment of the cornea by subconjunctival injections of irritating substances. Protein shock was tried by one author.

A variety of surgical procedures have been performed, but usually with no more success than met the medical measures. Superficial curettage of the cornea was the first operation employed (Haab, Dimmer

Groenouw), but most authors reported unfavorable results. Verhoeff,[73] however, reported beneficial results from this procedure in 3 cases. Optical iridectomy has been done in a considerable number of cases. Bücklers examined several patients who had had optical iridectomies but found the visual acuity unimproved and the patient more uncomfortable because of the dazzle and colored vision that ensued. Other operations that have been tried are paracentesis, cauterization, sympathectomy, grafting of mucous membrane from the lip and corneal transplantation. Although it is commonly thought that the dystrophy eventually invades the graft, Franceschetti and Streiff [74] favored this type of operation. Keratoplasty was performed on one eye in each of 3 of the cases reported in the present paper, with favorable results in 2 cases to date, but there is no assurance that the degeneration will not invade the transplanted tissue in time.

REPORT OF CASES

CASE 1.—*History.*—Mrs. V. F., a white woman aged 35, came to the department of ophthalmology of the Vanderbilt Clinic on March 5, 1947, with the request that her 2 year old son (case 2) be treated for an hereditary corneal disease. She stated that her father, one sister, one brother and she herself had had some type of chronic corneal disease as long as she could remember. Figure 1 is the pedigree of this family, showing the afflicted and the nonafflicted members. She said that all 4 of them had been "doctoring" for this ocular trouble all their lives, but all forms of therapy had been unsuccessful. She was greatly upset that her young son began to show evidence of the same process.

Mrs. V. F.'s ocular disease began at the age of 3 months, according to her mother, with recurrent attacks of "inflammation of the eyes," lasting from two to four days. The attacks evidently consisted of conjunctival injection, tearing and photophobia. For many years the episodes recurred about once a month, but since her reaching maturity they had become progressively less frequent. At the time of this report, she had an attack about every six months. The last one was approximately six weeks before her visit to the clinic. She stated that with the passage of time the attacks seem also to have become less severe.

The patient was unable to date exactly the beginning of her loss of vision. She stated that vision had gradually, but constantly, decreased through her school years. She was able to read through the grade school years and finished grade school satisfactorily. She could not see well enough to go on to high school and has not been able to read print of any size for the past fifteen years.

During her youth she was a frequent patient at two of the larger eye clinics on the eastern coast and at various other general clinics. She stated that she had had an intensive laboratory investigation, including blood tests, cutaneous tests and roentgenographic studies of the chest, but that no cause for her disability had been found.

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73. Verhoeff, F. H., discussion on Lloyd,[50] p. 125.

74. Franceschetti, A., and Streiff, E. B.: Hereditary and Constitutional Dystrophies of the Cornea, in Ridley, F., and Sorsby, A.: Modern Trends in Ophthalmology, London, Butterworth & Co., Ltd., 1940, pp. 419-420.

Her general medical history was not unusual. She had had measles and mumps as a child, and mild sinusitis for many years, without operation on the sinuses. Her appendix was removed in 1940. She had nephritis in 1945; there were no sequelae. Her menstrual history was within normal limits. She had two miscarriages before her baby was born. She stated that they were spontaneous, and she could give no contributory data. She had a normal pregnancy and delivery in 1945, uncomplicated except for the mild nephritis.

Ophthalmologic Examination.—Vision: Vision was limited to counting fingers at 1 foot (30 cm.) in her right eye and to perception of hand movements at 1 foot in her left eye. Light projection was accurate in both eyes. The conjunctivas and lids were normal in appearance. Tension was normal to palpation in both eyes.

Corneas: Macroscopic examination revealed diffuse white opacity of almost the entire cornea of each eye. The opacification was so dense in the pupillary area that the iris and the pupil could not be seen. Peripherally, there was a band, about 1 mm. in width, adjacent to the limbus, which was considerably clearer than the central portion of the cornea. The iris could be seen through this portion of the

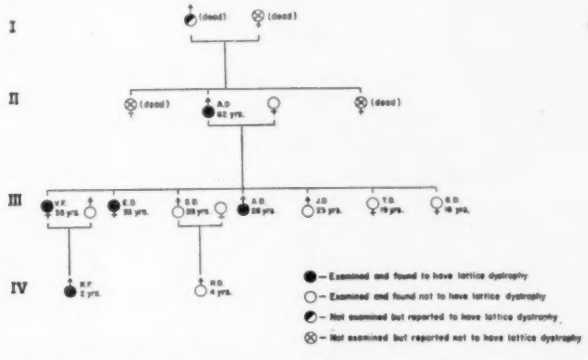

Fig. 1.—Diagram showing the pedigree of the afflicted family.

cornea and appeared to undergo normal movements when light was flashed into the eye. With the loupe and with good reflected illumination, a fine network of white lines, with many fine white dots in the interstices, could be seen. Viewed in this manner, the opacity gave one the impression of looking at a cobweb. The corneal sensitivity was moderately reduced in the left eye and greatly reduced in the right eye. There was no staining of the epithelium with fluorescein.

On microscopic examination with the slit lamp, the lattice-like network was not so obvious. In any one part of the beam a few lines were seen. The lesion consisted mainly, however, of myriad discrete, white deposits in all layers of the cornea, being much heavier in the anterior third than posteriorly. Here and there, larger deposits, which seemed to be accumulations of the smaller dots, were visible. The small, discrete dots were seen in the epithelium, but no lines were apparent there. The lines showed no definite pattern but seemed to run in all directions; some branched dichotomously, and all appeared to consist of the same refractile substance as the dots. It was difficult to study the lines with direct illumination; they were best seen with diffuse reflected light and were seen more easily in the peripheral parts of the opacity, where the iris began to show through. No blood vessels were seen in any portion of the cornea of either eye. The surface of the

epithelium was smooth, and there were no protrusions or breaks in its contour. However, its luster seemed much decreased. Figure 2 *A* is a drawing of the cornea of the right eye of this patient as seen with the slit lamp.

The anterior chamber and lens could not be observed in either eye because of the opacities in the cornea. The pupils, as seen through the periphery of the cornea, seemed to possess normal reactivity. The fundi could not be visualized. Transillumination showed nothing abnormal in either eye.

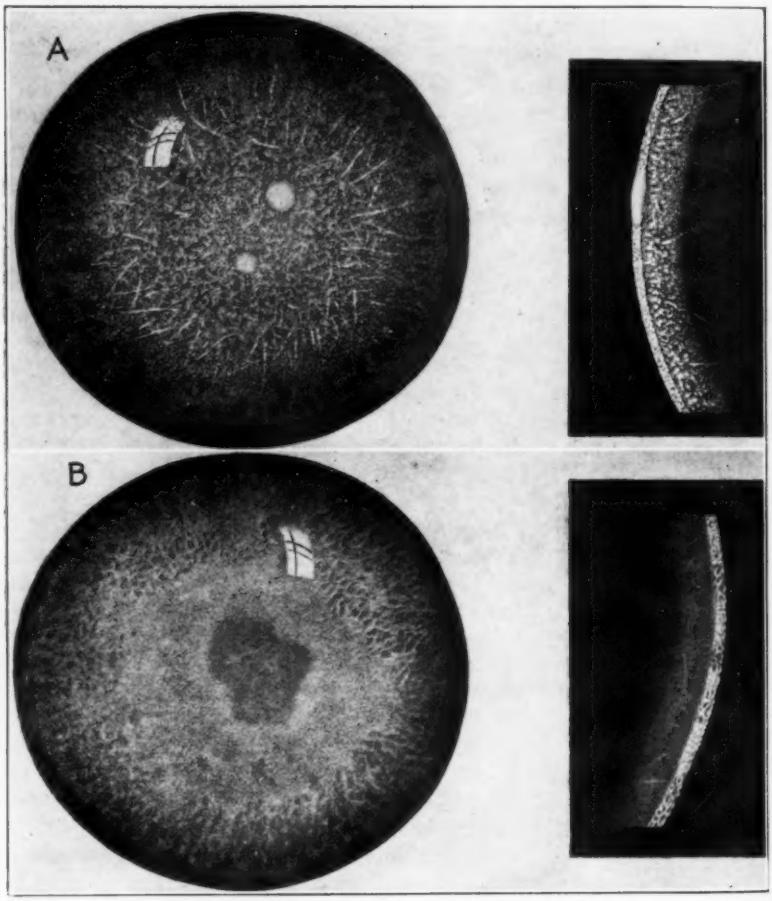

Fig. 2.—*A* (case 1), drawings of the cornea of the right eye taken with the slit lamp. *B* (case 3), drawings of the cornea of the left eye taken with the slit lamp.

A diagnosis of corneal dystrophy of the Haab-Dimmer type was made. Corneal transplantation, with a guarded prognosis, was suggested and was accepted eagerly by the patient.

Manifest refraction was —1.00 sph. ⌒ —3.50 cyl., axis 15 in the right eye; she read the 10/200 line with this eye. Vision in the left eye was not improved with lenses; she read the 2/200 line. There was no further improvement with the pinhole disk.

Operation and Subsequent Course.—On June 2, 1947, the patient was admitted to the Institute of Ophthalmology for cornea transplantation. General physical examination at that time revealed no defects except the corneal dystrophy. On the day following admission, a 5.5 mm. penetrating keratoplasty was performed, a specimen 5.5 mm. square being removed. The specimen was sent to the pathologic laboratory for sectioning, but the final result was not satisfactory. It was evident, however, that this specimen showed the same type of pathologic changes as are described in case 4. When the sutures were removed, one week after operation, the anterior chamber was flat and the iris was adherent to the graft nasally. The graft was flat but cloudy. Separation of the adhesions of the iris was then performed by means of cyclodialysis approach, and a conjunctival flap was brought down over the cornea. When the flap receded, the graft was clear, but the anterior chamber was still flat. There was no evidence of a leak with the fluorescein test. On her discharge from the hospital, six weeks after the keratoplasty, the anterior chamber was still flat, and there were anterior synechias below and temporally. Vision was not determined at this time.

She was readmitted to the hospital, and another synechiotomy (by cyclodialysis approach) was attempted on Aug. 25, 1947. The synechias recurred, however; the anterior chamber remained filled with blood, and secondary glaucoma ensued. On Sept. 3, 1947, a cyclodiathermy operation was performed. The tension remained within normal limits after this procedure, and the patient was again discharged. At the time of her most recent visit to the clinic (June 7, 1948), a ciliary staphyloma was developing in the eye which had been operated on; the graft was opaque, and there was no light perception.

Case 2.—R. F., a 2 year old white boy, the son of Mrs. V. F. (case 1), began to have attacks of "sore, red eyes" soon after his birth, his mother stated. The attacks, which consisted of pain in the eyes, lacrimation and severe photophobia, lasted from two to four days and recurred every three to four weeks. The attacks were usually first noticed in the morning, on rising. The child would not open his eyes, but kept them tightly closed for the duration of the episode, and insisted that all the window shades in the room be drawn. He preferred to stay in bed, had no appetite and was very irritable during the attack, although he was normally a pleasant child.

Careful examination was impossible at the first visit to the clinic because of lack of cooperation on the part of the child. However, he was "mummified" on the examining table; "pontocaine" (tetracaine U. S. P.) was instilled into the conjunctival sacs, and his eyes were opened by means of lid retractors. With a loupe, it was seen that he had some type of corneal opacity in both eyes, but the exact nature of the lesions could not be determined. He was referred to the department of pediatrics for a general examination, and his mother was requested to bring him to the hospital during one of his "attacks" for examination under ether anesthesia.

General physical examination by the pediatrics department revealed an entirely normal, well developed, well nourished, attractive-appearing child, without defect except for his eyes. The blood count and urine were normal. The Schick, Mantoux and Kline tests gave negative reactions.

Two weeks later, the child was brought to the clinic during an attack and was admitted to the Institute of Ophthalmology for observation and examination.

Ophthalmic Examination.—No visual test was obtained because of the patient's age and condition. According to his parents, he had no apparent visual difficulty except during his attacks. Both eyes were tightly closed, and he strongly resisted any attempt to open them. With the aid of tetracaine and lid retractors, a brief survey was made. The palpebral conjunctiva was moderately injected. The bulbar conjunctiva was white, and there was no ciliary congestion. The corneas appeared grossly clear. The anterior chambers were clear and of normal depth. Pupillary responses were normal. The eyes were straight, and the excursions seemed full. The fundi could not be visualized.

The patient was then given ether anesthesia by the open drop method in the treatment room. As soon as he was in deep anesthesia, he was held up before the corneal microscope by a nurse and the anesthesia continued as well as possible.

The central portion of each cornea was found to contain a fine network of white lines, in the interstices of which were a number of minute, discrete, white dots of a refractile substance. The process involved the whole cornea except for a clear area around the limbus. The deposits appeared to be subepithelial and were limited to the anterior third of the cornea. The size of the deposits was not constant: Most of them were fine and of approximately the same size and shape; a few were several times as large as the average. These larger deposits, in some cases, seemed to invade the epithelium. No blood vessels were seen in either cornea. The surface of the epithelium appeared normally smooth and regular except for one area near the center of the cornea in each eye, where the surface looked rough and broken. This rough spot was superimposed on a large, fresh-looking, yellowish deposit that protruded into the epithelium from the superficial layers of the stroma. On completion of examination with the slit lamp, the child was placed on an examining table and fluorescein instilled into each eye. The rough areas previously seen with the microscope stained a bright green.

The lines in the cornea were seen much better in this patient than in his mother (case 1) because there was much less deposition of the foreign material in the cornea. Whereas the round deposits in the mother's cornea were so numerous as to form an almost homogeneous mass in the center, they were discrete and scattered in the son's. The iris and pupil could easily be seen in the boy, and they provided a dark background that helped to clarify the lines and deposits. Viewed against this background, some of the lines gave the effect of a hollow tube, described by Bücklers and Berliner. These appeared as double lines, with an optically clear interval between. The lines crisscrossed over the cornea in no definite pattern: Some were long; some were short; some branched, and some did not. Macroscopically, neither the lines nor the nodules could be seen.

The patient recovered from the anesthesia uneventfully, and the following day he was discharged from the hospital. A diagnosis of the Haab-Dimmer type of corneal degeneration was made. Treatment can be only palliative in patients of this age group.

Case 3.—Miss C. D., a white woman aged 32, is the sister of Mrs. V. F. (case 1). According to her mother, she began to have attacks of red, sore eyes at about 5 months of age. These had recurred regularly at monthly intervals for many years. The patient attended regular grade school and completed the eight grades satisfactorily, although she attended sight conservation class for one year (fifth year). In her early teens, she was able to read books and newspapers. She wore glasses through the school years and expressed the belief that she was near sighted. When 18 years of age, the patient inadvertently took too many

sleeping tablets and had to be taken to the hospital to have her stomach "washed out." She dated her loss of vision from that episode, stating that her visual acuity deteriorated rapidly the following year. She was taken many times to various ophthalmologic clinics, together with her sister, but had had progressive loss of vision for the fourteen years prior to her present visit.

Her general medical history was noncontributory so far as the disease of the eyes was concerned. She had measles and mumps as a young child, and bronchopneumonia at 5 years of age. An appendectomy was performed in 1933, and operations for bilateral hallux valgus were done in 1939. In 1940 an optical iridectomy was done on the left eye, without appreciable increase in vision. In 1942 an ovarian cyst was removed, and in 1945 bilateral partial oophorectomy and salpingectomy were performed. She stated the belief that the latter operations were for adhesions.

Ophthalmologic Examination.—Vision was limited to perception of hand movements at 2 feet (60 cm.) in each eye. Light projection was accurate in both eyes. Tension appeared normal in both eyes on palpation. Transillumination revealed nothing abnormal in either eye. The conjunctivas and lids were normal in appearance.

Corneas: Macroscopic examination revealed a diffuse white opacity of most of the cornea of each eye; peripherally there was a narrow clear band. The opacity in the pupillary area was so dense that neither the iris nor the pupil could be seen. The iris could be observed through the peripheral clear area, and apparently the pupillary reactions were normal. A wide iridectomy, from 12 to 3 o'clock had been performed on the left eye. The corneal sensitivity was considerably reduced in each eye. There was no staining of the epithelium with fluorescein.

With the corneal microscope, the same lattice-like network of lines and dots was seen in this patient's corneas as was exhibited by her sister. The lesion was so dense centrally that it assumed the appearance of a homogeneous white mass. As one left the central area, however, the discrete, white deposits become less concentrated and the lines become evident. In the portion of the periphery which appeared clear and transparent grossly, the lines and dots were greatly reduced in number but were still present. As in the previous 2 cases, the foreign material was largely found in the anterior third of the cornea, the stroma becoming progressively clearer as one looked posteriorly. No blood vessels were found in either eye. Figure 2 *B* is a drawing of the cornea of the left eye of this patient made with the slit lamp.

Manifest Refraction: There was no improvement with lenses in either eye. She saw only hand movements with either eye. There was no further improvement with pinhole disks.

A diagnosis of familial corneal degeneration of the Haab-Dimmer type was made. The case was considered unfavorable for corneal transplantation, but an attempt to improve the patient's vision by the operation was considered justified because of the degree of her visual loss.

Operation and Subsequent Course.—The patient was admitted to the Institute of Ophthalmology and a keratoplasty performed on her right eye, a specimen 5 mm. square being removed. Unfortunately, the tissue was not saved for pathologic examination. During her convalescence from the operation, she had one of her "attacks" in the left eye. Examination revealed mild conjunctival injection, tearing and moderate photophobia. Staining with fluorescein revealed

an irregular abrasion of the center of the cornea, very similar to the one seen in her nephew (case 2). Examination with the slit lamp showed a large, fresh-looking, amorphous, yellow deposit in the epithelium and anterior layers of the substantia propria. The remainder of the corneal surface was unchanged. This ulceration healed over in three days, and her symptoms disappeared.

On her discharge from the hospital, vision in the right eye was 20/70 with a pinhole disk. Figure 3 contains photographs of the eyes before and four weeks after the operation. Two months after discharge, manifest refraction was —6.00 sph. ⌒ —6.00 cyl., axis 103 in the right eye. She read 20/50 easily. Four months after the operation, the graft was still clear and vision with correction unchanged.

Eighteen months after operation, vision in the right eye was reduced to 12/200, with a correction of —9.00 sph. ⌒ —6.00 cyl., axis 105. The graft was still clear but evidenced a tendency to bulge forward.

Case 4.—Mr. A. D., a white man aged 61, the father of the patients in cases 1 and 3, was born in Italy but had been in the United States for forty-three years.

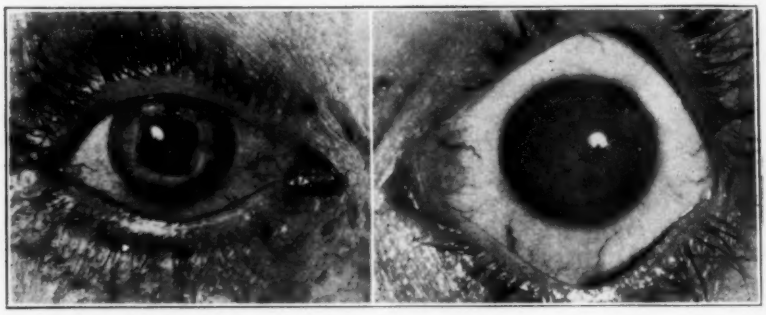

Fig. 3 (case 3).—The right eye, four weeks after operation. The left eye is shown for comparison because no photographs were taken of the right eye before operation.

He remembered that his father always suffered from "bad eyes," and he expressed the belief that this was due to the same type of disease that he and 4 members of his family now had. The father died forty-one years ago. The mother was not afflicted.

The patient's story was very similar to that of his daughters. He had had frequent attacks of "sore, red eyes" ever since he was a baby. During his childhood, they recurred every three or four weeks and were so painful that "he threw himself on the ground and cried." He was uncertain about the date of his beginning to lose his vision, but he remembered that he had visual difficulty at about 21 years of age and that at 30 he was going to doctors for glasses to improve his sight. For the past thirty years, visual acuity had undergone a steady, progressive decrease. He had always worked as a laborer.

There was nothing remarkable in his general medical history. He had had the usual childhood diseases, but did not remember specifically which. He had one attack of pleurisy when a young man but had had no other evidence of tuberculosis. Bilateral optical iridectomy was performed in 1940. He had had bronchial asthma for the past ten years.

Ophthalmologic Examination.—Vision was counting fingers at 2 feet (60 cm.) in the right eye and was 4/200 in the left eye. Light projection was accurate in both eyes. The tension was normal to palpation in both eyes. Transillumination revealed nothing abnormal in either eye. The conjunctiva and lids were normal in appearance.

Corneas: Macroscopically, there was a diffuse white opacity of each cornea, similar to that in the previous cases. In one feature it differed from that of the daughters. A group of prominent large white lines ran radially and roughly

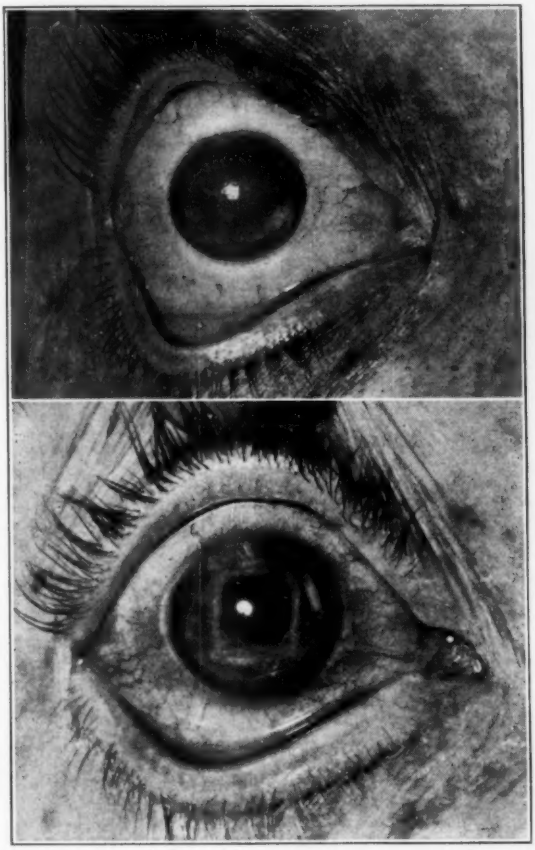

Fig. 4 (case 4).—Photographs of the right eye before and one month after operation.

parallel in the upper part of each cornea. These seemed exactly like the other lines when studied microscopically, except that they were larger and were easily seen with the naked eye. The periphery was again relatively clear. The corneal sensitivity was reduced in both eyes. There was no staining of the epithelium.

Microscopically, the lattice effect of the lines was more obvious in this patient than in the others. There were many lines, easily seen with reflected illumination and a low power objective in the microscope, which ran together to form a lacelike design throughout the cornea. The lines and dots were again found predominantly

in the anterior third of the corneal stroma. The center contained the greatest concentration of the foreign material, and it was so dense that the pupil could not be seen. Peripherally, the iris could be seen, and apparently reacted normally. The results of wide basal iridectomies could be made out above in each eye. No blood vessels were seen in either eye. The surface of the epithelium was normally smooth, but lacking in the usual luster of healthy epithelium.

Manifest Refraction: Vision was not improved with lenses, and was limited to hand movements in each eye. There was no further improvement with pinhole disks.

Operation and Result.—A diagnosis of the lattice type of corneal dystrophy was made. The patient was anxious to have a transplantation because of the good results in his daughter's case. He was admitted to the Institute of Ophthalmology, and keratoplasty was performed on his right eye, a specimen 5 mm. square being removed. The pathologic specimen was carefully preserved and sent to the laboratory for examination. Figure 4 shows photographs of this patient's right eye before and one month after the operation. Two months after his discharge, manifest refraction for the right eye was — 5.50 sph. ⌒ — 1.50 cyl., axis 155, and he read 20/50 easily. This correction was prescribed, and three months after operation the graft was still clear and corrected vision unchanged.

Fourteen months after operation, the patient was complaining of decreasing vision. Vision in the right eye (with his glasses) was 20/100. Refraction was not obtained prior to publication.

Pathologic Examination.—The specimen was a section of cornea, about 5 mm. square. The posterior surface had shrunken, however, so that it is only about 2 mm. long. This had caused the ends of the epithelial surface to bow posteriorly, in the manner typical of transplantation specimens. The cornea appeared much thicker than normal, but this may have been an artefact, due to the wrinkling of the posterior layers. Figure 5 shows three sections of the specimen stained with hematoxylin and eosin, the Masson trichrome method and the Van Gieson method.

The epithelium was of irregular thickness (fig. 5 *A*). In some places it consisted of only three layers of cells, and in others it was stratified and composed of eight to ten layers. In the thickest places, the basal layer was composed of high columnar cells, which were pale and appeared hydropic. In the area of intermediate thickness, the basal layer was made up of cuboidal cells, similar in appearance to the columnar type. In the thinnest parts of the section, there was no basal layer; the epithelium consisted of merely a few layers of flat, horizontal, squamous-like cells. In the places where the columnar and the cuboidal basal layers were present, there were no intermediate, or wing, cells of Salzmann; the transition was abrupt, from tall to flat cells. The normal architecture of the epithelium was totally destroyed throughout the sections.

In the sections stained with the Masson trichrome method, there was an unusual staining arrangement of the epithelium. The superficial layers of the epithelium had taken a deep red stain, identical with the red-staining material in the anterior

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Fig. 5 (case 4).—Low power magnifications of three sections from the pathologic specimen obtained. *A*, section stained with hematoxylin and eosin, showing well the irregularity of the epithelium. *B*, section stained with the Masson trichrome stain, showing general distribution of the foreign material; the dark anterior portion of the cornea stained almost solidly dark red with this stain. *C*, section stained with Van Gieson's stain, showing little at this magnification.

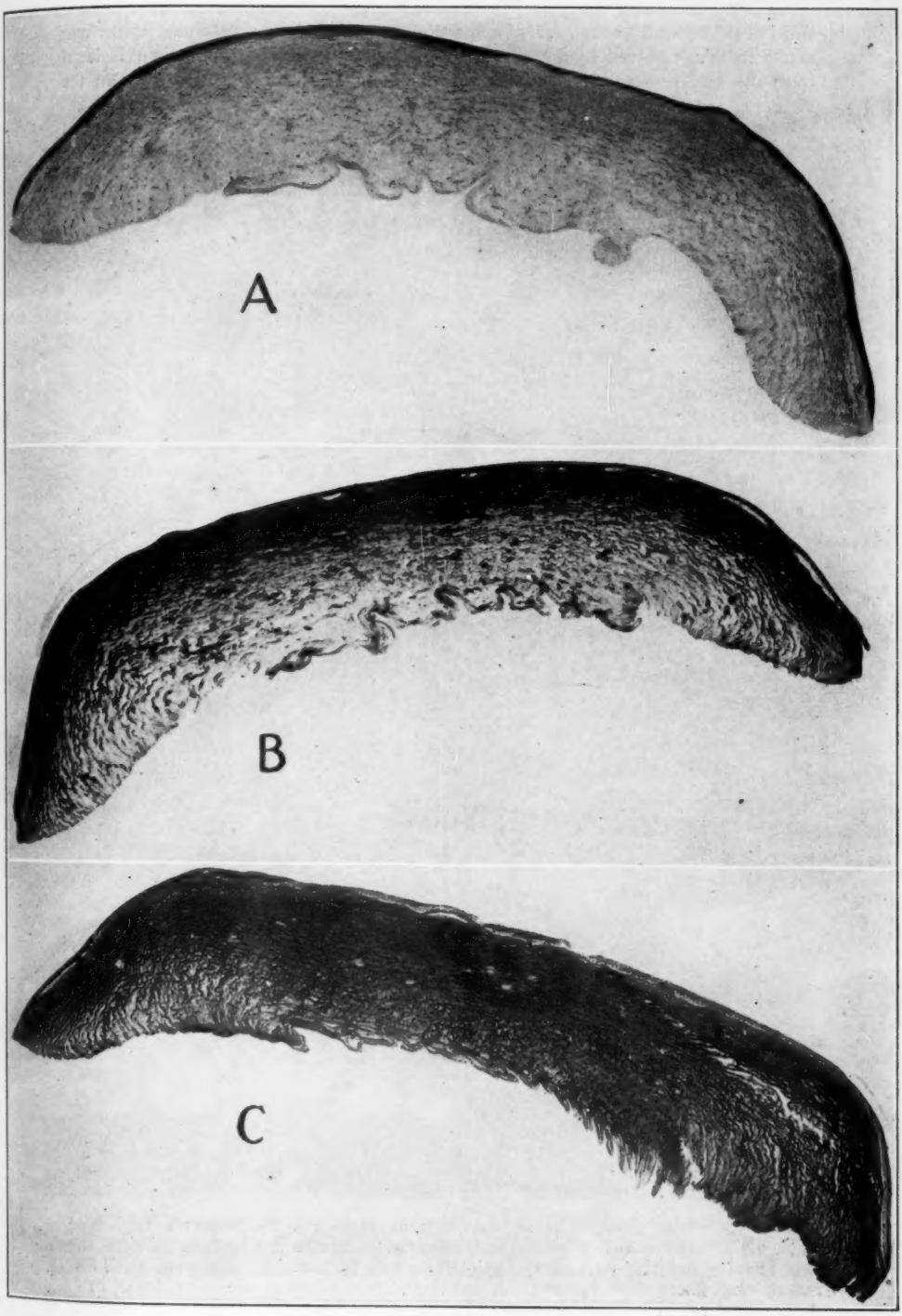

Figure 5

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third of the corneal stroma. Here and there, bridges of similarly staining epithelium connected the two red layers, leaving islands of blue-staining epithelium isolated from the surface (fig. 6 *1a*). This peculiar staining pattern was not seen in the slides stained with the Van Gieson method or with hematoxylin and eosin.

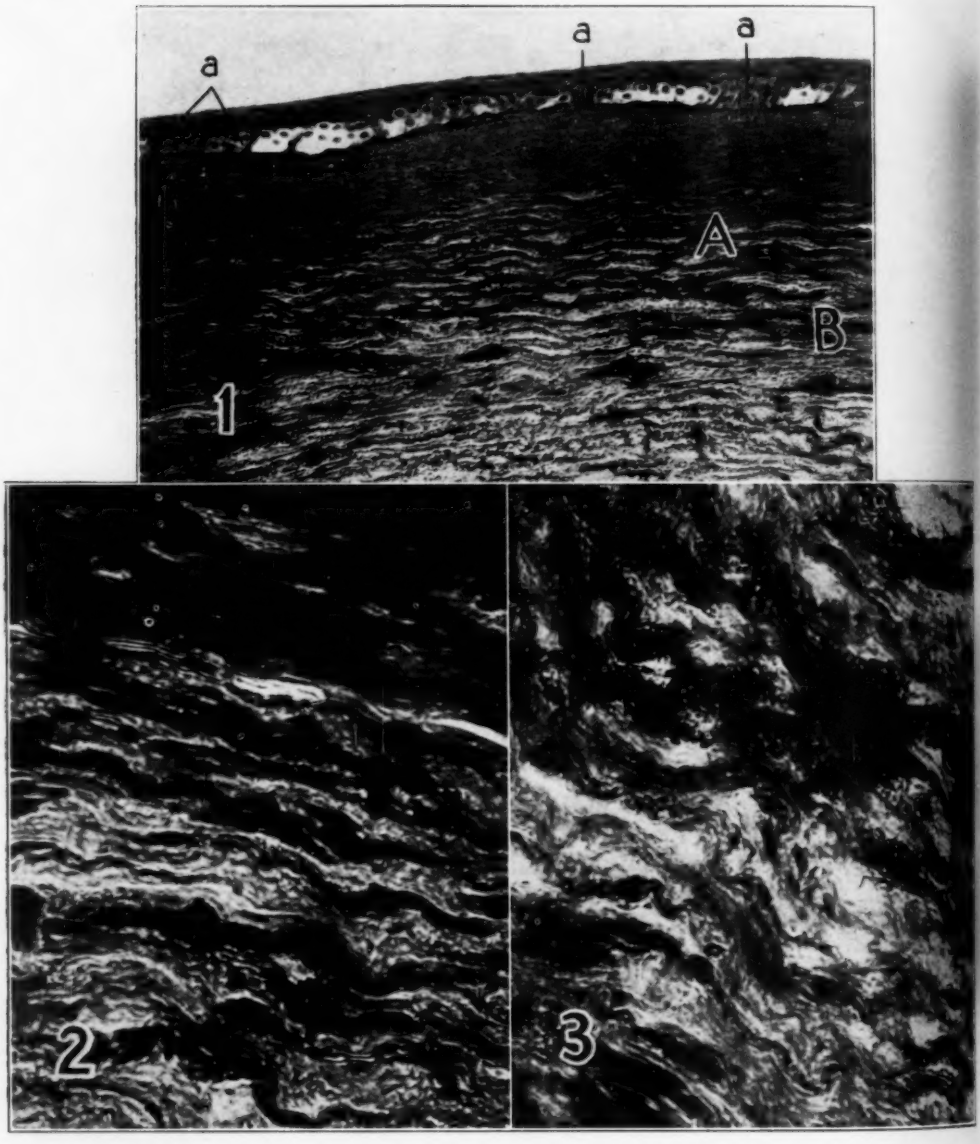


Fig. 6.—Photomicrographs of the sections stained with Masson's trichrome stain. *1*, anterior two thirds of this section; *a*, points to the bridges between the deep-staining anterior part of the epithelium and the stroma. Many of the long, red-staining fibers show up well. *2*, a magnification of the stroma at point *A* in *1*, shows the large red fibers and some of the extralamellar deposits; *3*, a magnification of the stroma at point *B* in *1*, shows the small intralamellar deposits.

At intervals "bumps," or protuberances, of corneal stroma extended into the epithelium, seeming to push the epithelial cells to each side. These swellings were laminated structures, made up of alternate layers of corneal lamellas and the foreign deposition seen throughout the sections. Figure 7 *A*, a photomicrograph, shows two of the "bumps" from a slide stained with Van Gieson's stain, as well as the alternate red and yellow bands.

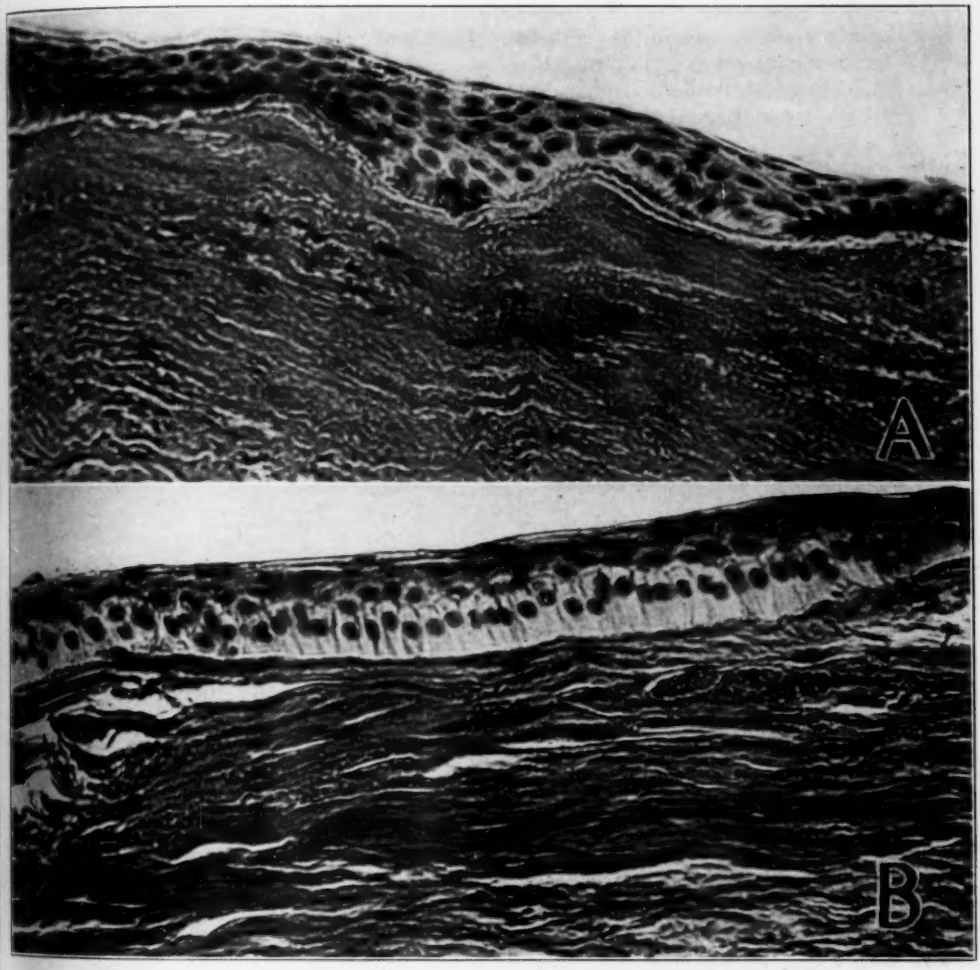


Fig. 7.—Photomicrographs of the sections stained with Van Gieson's stain. *A* shows two of the "bumps" bulging forward into the epithelium, with their laminated structure; *B*, columnar epithelium with superimposed flat, squamous cells and no intermediate layer.

Bowman's membrane could not be seen in any of the sections; at least there was nothing resembling a normal membrane. A line of demarcation could be made out, separating the epithelium from the substantia propria, but it was very irregular and was made of the foreign substance which stained red with the trichrome method and yellow-orange with the Van Gieson method. The irregular-

ities of this line were due not to epithelial downgrowths, but to forward protrusions from the stroma. One received the impression that the stroma was sending forward tonguelike processes into the epithelial layer.

The anterior third of the cornea contained most of the pathologic change. With the trichrome stain, this portion was seen to take a deep red color. It consisted of a dense network of wavy, red bands (fig. 6*2*). In the interstices of this net were seen thin blue bundles, and here and there were islands of blue bundles. The red-staining bands were not homogeneous; they had a fibrillar structure. No nuclei could be seen in the red bands. They appeared to be corneal lamellae but were slightly irregular in their course.

The middle third showed less dense and shorter bands, fewer than in the anterior third, and interspersed with small, irregular patches of the same red substance

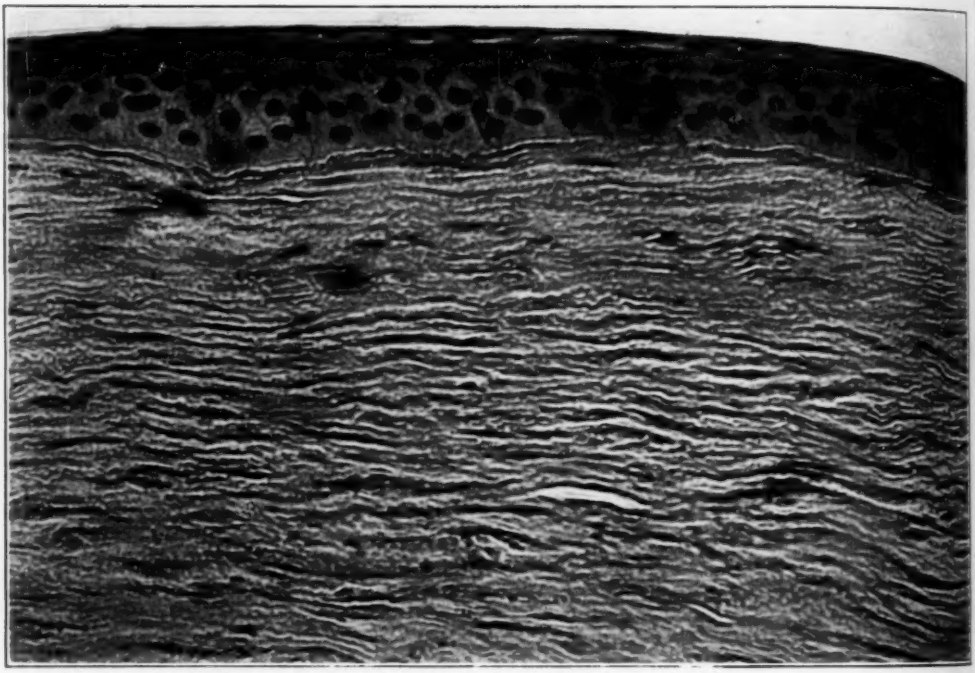


Fig. 8.—Photomicrograph of a section stained with hematoxylin and eosin. Note the apparent scarcity of the abnormal fibers in the anterior third, as compared with the appearance of the trichrome stain.

(fig. 6*3*). These deposits were seen both inside and outside the corneal lamellas. The larger deposits were observed to be extralamellar. The smaller, intralamellar, deposits might number eight to ten or more, were arranged in a row and looked somewhat like peas in a pod. These would seem to represent an earlier stage of degeneration than the solid red lamellas of the anterior third of the stroma. The red deposits were not strictly homogeneous, appearing granular in many places.

The posterior third of the stroma was highly disorganized and wrinkled. It is probable that much of this was artefact, due to shrinking and wrinkling of Descemet's membrane. The same red deposits were found here, but they were even smaller and fewer than in the middle third. They could be found all the way back to Descemet's membrane. No long red fibers were seen in this portion.

Descemet's membrane appeared normal and had retracted into several folds, as it does when incised. The endothelium was bunched in the folds of Descemet's membrane. In some places it stained red in the trichrome sections, contrary to what one would expect. Some of the endothelial cells were larger than normal.

With the Van Gieson stain, the abnormal deposits were seen to take a deep yellow color. Again, the deposits were heaviest in the anterior third, becoming fewer and smaller as one looked posteriorly. Intermingled with the yellow bands were the corneal lamellas, now staining red. With this stain the corneal stroma could be seen to have a dearth of nuclei: in some areas under the epithelium one saw no nuclei at all. In other places, the nuclei were present but stained faintly. Several large, discrete, rounded, yellow deposits could be seen in the anterior half of the stroma, in the interlamellar spaces. The yellow material could also be seen posterior to Descemet's membrane, but with this stain the endothelium looked fairly normal. The outstanding difference between the Van Gieson and the trichrome sections was the fact that the anterior third of the stroma did not show nearly as much yellow deposit with the Van Gieson stain as it did red with the trichrome stain.

The material, so well seen with the trichrome and the Van Gieson stain, was scarcely visible with hematoxylin and eosin. Some granular deposits were seen in the deeper layers (fig. 8). These were pink and hyalin-like. Some areas were devoid of nuclei. There some homogenization of the lamellas in places anteriorly. The "bumps" of stroma protruding into the epithelium could be seen well with this stain.

Frozen sections were prepared and stained with nile blue sulfate and sudan III for fat, and with the Schultz stain for cholesterol. All gave negative results. No evidence of fatty degeneration could be found.

CASE 5.—A. D., a white man aged 24, was the son of the patient in case 4. His ocular trouble began in the first six months of life, and during his early years he suffered from attacks of "sore eyes" at approximately monthly intervals. He also went with his father and sisters to certain of the large clinics of the eastern coast.

The patient attended the first four grades of school in the usual manner and stated that he could see fairly well then. Beginning with the fifth grade, however, he attended sight conservation classes and continued to do so throughout the rest of grade and high school. He stated that he was still able to read large print after he had finished high school. He had never worn glasses but had had exotropia as long as he could remember.

During the past few years before he came to the Vanderbilt Clinic, his attacks of "sore eyes" had become less frequent, then occurring only once or twice a year. They had also decreased in severity. Nevertheless, he had noted an increased visual loss in the past four years. When 20 years old, he could still play cards, but he could not do that at the time of examination. Neither could he read any print. He was employed as a pipe fitter and said that he got along satisfactorily at that job. He identified his tools and pipe fittings by touch. He saw well enough with the left eye to get around alone.

The patient's general medical history was essentially noncontributory. He had had two childhood diseases but did not remember which. He broke his arm in an automobile accident when 12 years old. He had had no operations. He had been married for three years and had no children.

Ophthalmologic Examination.—The patient was a good-looking, healthy-appearing man, with no visible defect except a divergent squint and the corneal dystrophy.

Vision was perception of hand movements at 2 feet in the right eye and 15/200 in the left eye. Light projection was good in the right eye. Tension was normal in

both eyes. Transillumination revealed nothing abnormal in either eye. The conjunctivas and lids were normal in appearance.

Corneas: Macroscopically, there was a gray, grill-like opacity of the cornea in each eye. The opacities presented by this patient were not dense and white in the center, as in the case of his sisters and his father. The pupil and the iris could easily be seen through the opacities, which had the appearance of fine lace. The peripheral clear areas, so distinctive in the other cases, were narrower (about 0.5 mm.) and less distinct in this patient. Corneal sensitivity did not seem to be appreciably decreased, and there was no staining with fluorescein.

Microscopically, with the slit lamp, the lattice-like network was obvious in both eyes. Almost the whole cornea was crisscrossed in every direction with a multitude of fine, gray lines. In the interstices were seen many fine, discrete, round deposits, but no large, conglomerate ones. Although many more lines were found in his corneas than in his sisters' and his father's, the concentration of dots was much less. His condition seemed to be in an intermediate stage between the child's (case 2) and the disease of the other adults. The foreign material was again chiefly located in the anterior portion of the cornea. No blood vessels could be seen. The corneal surfaces were smooth and unbroken by indentations or protuberances. The luster of the epithelium seemed about normal.

The anterior chambers appeared normal in every way. The pupillary reactions were full and equal. The fundi could not be visualized, but a red reflex was present in each eye. He had a divergent squint of about 45 D., with the left eye fixing. Excursions were normal.

Manifest Refraction: Vision was not improved with lenses in either eye. It was limited to perception of hand movements at 2 feet in the right eye and to 15/200 in the left eye. There was no further improvement with pinhole disks.

A diagnosis of lattice corneal dystrophy of the Haab-Dimmer type was made. It was felt that the patient had amblyopia ex anopsia in the right eye; in view of that fact, keratoplasty was not recommended for the left eye. He was, however, admitted to the Institute of Ophthalmology for a resection and recession on the right eye for cosmetic purposes. The result was satisfactory cosmetically.

One year later, vision in the left eye was reduced to 3/200 and the patient was having difficulty with his work. On July 7, 1948, a lamellar (nonpenetrating) corneal transplantation was performed on the right eye, and on August 11 a similar operation was done on the left eye. In this procedure the anterior chamber is not incised; a circular disk of corneal tissue is removed from the anterior one half or three quarters of the cornea, and a similar disk is taken from the donor eye and sutured into this defect. Two months later, these grafts were clear, and the patient was able to read the newspaper and telephone book easily (with the left eye, of course). It is too soon, however, to evaluate the result of this procedure.

SUMMARY

The lattice type of corneal dystrophy is a chronic, slowly progressive, familial disease of the cornea, inherited dominantly. It begins in the first decade of life, and usually in the first few months. It is characterized in youth by frequent recurrent erosions of the corneal epithelium, associated with severe photophobia, lacrimation and mild conjunctivitis. In the adult years, the recurrent attacks become less frequent and milder, but there is progressive loss of vision. The lesion is always bilateral and occurs as frequently in females as in males. The corneal sensitivity is greatly decreased in advanced cases.

Macroscopically, the corneal lesion is a diffuse opacity, resembling a spider web, involving the whole cornea, except the peripheral 1 or 2 mm. In early cases, interlacing gray lines and fine nodules may be seen with the naked eye or the loupe. Microscopically, the beam of the slit lamp reveals many wandering lines, with a myriad of fine deposits in the interstices, involving all the layers of the cornea, but with a great preponderance in the anterior third. No blood vessels are found in the stroma in uncomplicated cases. Examination of the cornea during one of the "attacks" reveals ulceration of the epithelium over a large mass, or nodule, of the foreign material.

The etiologic factor is unknown. It has been variously suggested that the lesion is due to a nutritional disturbance, a glandular disturbance, tuberculosis, primary degeneration of connective tissues, abiotrophy, degeneration of the corneal nerves or aneurysm of the limbal blood vessels. There is no concrete substantiation for any of these theories.

Pathologically, a hyalin-like material is observed deposited within and without the corneal lamellas and in the epithelium. The intralamellar depositions are tiny and may be found in a row inside the individual fibers. The larger deposits are extralamellar and acquire a considerable size. It is suggested that they are accumulations of the smaller deposits that have broken out of the degenerated corneal fibers. The depositions are concentrated in the anterior layer of the corneal stroma and become progressively fewer toward Descemet's membrane. Bowman's membrane is usually missing. The epithelium is completely disorganized architecturally and is very thin over the large protruding masses in the anterior layers of the stroma.

According to the classification of Bücklers and others, the lattice type of dystrophy is a distinct clinical entity. It is differentiated from the granular type of familial dystrophy by the presence of "lines" in the lesion, by the relatively early loss of vision and by defective corneal sensitivity. It is differentiated from the macular types of corneal dystrophy by the lines and the nodules, its central location in the cornea and its dominant inheritance.

The treatment of corneal dystrophies has always been unsatisfactory. There is no medical agent of any known value. Keratoplasty offers promise at present, but the prognosis is guarded until the permanent outcome of the graft is known.

Approximately 100 cases of this rare disease have been reported in the literature. This report adds 5 cases that fit into the clinical and pathologic pattern of the disease, including that of the youngest patient to be reported up to the present time.

Dr. Gustav Bethke made the drawings with the slit lamp, and Dr. Ludwig von Sallmann aided in the diagnosis and examination of the patients.

704 State Tower Building.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Anatomy and Embryology

THE LAMINA CRIBROSA AND ITS NATURE. M. WILCZEK, Brit. J. Ophth. **31:** 551 (Sept.) 1947.

Wilczek states that present knowledge of the lamina cribrosa and its function is based mostly on the work of Ernst Fuchs, as there have been no newer researches in this field. In order to be thoroughly acquainted with the structure of the lamina, its relations to the sclera and septums of the optic nerve and its function and importance, Wilczek studied histologic longitudinal and transverse sections of the lamina, not only of adults but of the newborn and embryos and of the cat, pig, horse and ape. His studies demonstrate that the cribriform lamina develops comparatively late and that its complete development is attained as late as the end of fetal life, or even the beginning of extrauterine life. Trabeculae of connective tissue grow into the nerve and the disk from all directions and from all available sources of connective tissue, namely, from the pia mater, from the sclera in the scleral canal and, as can be demonstrated in the series of transverse sections, also from connective tissue which accompanies the central vessels. These connective trabeculae form the septal network of the nerve. By their ingrowth, the nerve is supplied with vessels and its structure strengthened; delicate nervous tissue is connected with the pia mater, and the optic nerve inside the scleral canal is fixed to the sclera.

Wilczek considers fixation of the optic nerve in the scleral canal, i. e., in the place where the optic nerve is exposed to the great danger of being pulled, as one of the most important functions of the cribriform lamina.

He is convinced that there is no substantial difference between the lamina cribrosa and the septal system of connective tissue of the optic nerve. They actually form one common system, the parts of which can be differentiated only by their point of origin. In the scleral canal, trabeculae are thicker because they come from the sclera; in the nerve, they are thinner because they come from the pia mater.

The cribriform lamina is, then, not an independent structure but the foremost and strongest part of the septal system of connective tissue of the nerve. In his studies, Wilczek made a plastic model of the region of the eye, enabling him to visualize the relations in three dimensions.

W. ZENTMAYER.

Conjunctiva

RECESSION OF LIMBAL CONJUNCTIVA. M. LOMBARDO, Am. J. Ophth. **30:** 1109 (Sept.) 1947.

Lombardo suggests recession and permanent fixation of the circumcised margin of the limbal conjunctiva away from the cornea in the cure

of pannus. This results in disappearance of the pannus and permanent improvement of visual conditions, prevents corneal ulcerations and brings about deepening of the fornices.

W. S. REESE.

PRIMARY MENINGOCOCCAL OPHTHALMIA. F. N. SHUTTLEWORTH and J. G. BENSTEAD, Brit. M. J. **2:** 568 (Oct. 11) 1947.

Two cases of primary meningococcic conjunctivitis in school children in Leeds are described. In 1 case sulfacetimide (*p*-aminobenzene sulfamylacetylimide) was used locally, and in the second penicillin was applied locally, with good results. The importance of recognizing the meningococcus as a primary cause of conjunctivitis is emphasized. The authors note that meningococcic conjunctivitis predominates among males; that in nearly one-half the cases both eyes are involved; that corneal ulceration takes place in one sixth of the cases, but without permanent damage to the eye, and that meningitis is an unusual, but possible, sequel.

ARNOLD KNAPP.

Congenital Anomalies

TYPES OF CONGENITAL CATARACT. F. C. CORDES, Am. J. Ophth. **30:** 397 (April) 1947.

In this Sanford R. Gifford Memorial Lecture, Cordes discusses the embryology of the lens and enumerates the various types of congenital cataract; he also reviews the embryology of the vitreous and discusses retrolental fibroplasia and encephalo-opththalmic dysplasia.

W. S. REESE.

A CASE OF CONGENITAL VERTICAL SHORTNESS OF THE LIDS COMBINED WITH TETRASTICHIASIS. J. LANDAU, Brit. J. Ophth. **31:** 219 (April) 1947.

A case of congenital shortness of the lids in the vertical direction ("vertical shortness") combined with tetrastichiasis is described. There was a partial eversion of the cutaneous part of the upper lid margin. In spite of an existing lagophthalmos, the eyes remained free from irritation, possibly because of a coexisting hypertrichosis. In the sulcus subtarsalis a dark line was apparent, due to the hair follicles of the supernumerary cilia showing through the conjunctiva. These cilia have probably taken the place of the meibomian glands, occupying their ducts.

W. ZENTMAYER.

PERSISTENCE OF THE HYALOID ARTERY. E. V. BERTOTTO and V. ABREBANEL, An. argent. de oftal. **7:** 48 (April-June) 1946.

Two cases of persistence of the hyaloid artery are described. In the first case there was also a peripheral area of choroiditis, and in the second case, an area of pigmented choroiditis at the macula. The authors think that there may be a possible connection between the two conditions.

M. E. ALVARO.

Cornea and Sclera

XEROPHTHALMIA AND KERATOMALACIA IN CHILDREN. A. TUPAS, L. V. PECACHE and A. MELO, J. Philippine M. A. 23: 137-190 (April) 1947.

Tupas and his co-workers review observations in 97 cases of vitamin A deficiency with ocular manifestations. Vitamin A deficiency may be brought about in three ways: (1) through inadequate intake of the vitamin; (2) through deficient absorption and storage as a result of intestinal or hepatic derangement, and (3) through an increased demand for the vitamin, as during a period of rapid growth or of disease. In most of the cases observed by the authors, the ocular symptoms were caused by the second and third factors. In several instances admission to the hospital was sought not for the ocular lesion but for dysentery or bronchopneumonia. The ocular lesion, if complained of, was only a minor consideration. Night blindness and photophobia are early symptoms. Examination of the eyes may reveal xerotic conjunctiva and Bitot's spots. Keratomalacia is the advanced form of the ocular lesion due to vitamin A deficiency. It existed in 14 of the 97 cases reviewed. The authors emphasize the importance of early diagnosis and treatment to prevent blindness in infancy and childhood. Treatment consisted mainly in giving foods rich in vitamin A, such as egg, banana and liver. In cases in which the appetite had been impaired or completely lost, vitamin A concentrates and multiple vitamin preparations were given. The local application of vitamin A in oil to the eyes was also tried, with fairly good results.

J. A. M. A. (W. ZENTMAYER).

PHLYCTENULAR KERATOCONJUNCTIVITIS IN A YOUNG GIRL IN RELATION TO THE MENSTRUAL CYCLE. P. BARRAT and A. KOUTSEFF, Bull. Soc. d'opht. de Paris, November-December 1946, p. 100.

A girl aged 14 had recurrence of the lesion two or three days previous to each menstrual period. The reaction to tuberculin was positive locally but negative so far as the ocular or any general reaction was concerned. Therapy with tuberculin was of no avail, but injection of estrogen previous to the expected appearance of the lesion acted as a vaccine. This case is the only one of its type in the authors' experience.

L. L. MAYER.

CURE OF BLINDNESS OF FORTY-TWO YEARS' DURATION BY KERATOPLASTY. ANTONIO TORRES ESTRADA, Bol. Hosp. oftal. Ntra. Sra. de la Luz 3:245 (Jan.-Feb.) 1947.

The case is presented of a man aged 54 in whom lagophthalmos developed in both eyes as a complication of exanthematous typhus. The end result was total loss of vision in the right eye, due to corneal staphyloma, while the patient was able to distinguish only light, colors and, vaguely, very large objects with the left eye. The following year an iridectomy was performed on the left eye at 12 o'clock. The right eye was enucleated because of the staphyloma and recurrent attacks of inflammation. The left eye showed an extensive central adherent leukoma at the lower portion of the cornea, square and surrounded by a transparent zone, through which the iris could be seen. Keratoplasty

was performed, using Castroviejo's technic, and the dressings were removed in fifteen days. The postoperative period was satisfactory. Final visual results were 0.9 for distance and ability to read Jaeger type 1.

M. E. ALVARO.

Experimental Pathology

HISTOLOGIC STUDY OF EXPERIMENTAL CORNEAL TRANSPLANTATION. H. M. KATZIN and P. K. KUO, Am. J. Ophth. **31:** 171 (Feb.) 1948.

Katzin and Kuo summarize the literature on the histology of corneal transplantation, both human and experimental, and discuss the evidence in favor of true healing versus replacement of the graft.

Their experimental studies are presented, with sections showing normal healing as well as operative complications. Since corneal tissue is unique in its properties of transplantability, considerable emphasis is placed on this phase.

The authors believe that, in successful cases, the cellular elements of the transplant are replaced by the host, and that the intercellular structures of the graft are accepted and persist.

W. S. REESE.

General

AN OCULIST IN SWITZERLAND. J. FOSTER, Brit. J. Ophth. **33:** 83 (Feb.) 1948.

This is an interesting and informative account of the author's visit to the ophthalmic clinic at Basel, Schaffhausen, Zurich, Berne, Lausanne and Geneva. It contains a description of the newer methods of examination, operations and apparatus employed in the various clinics. The article does not lend itself to abstraction.

W. ZENTMAYER.

OCULAR ALLERGY. C. PAVIA, Rev. brasil. de oftal. **5:** 29 (Sept.) 1946.

The author presents 2 cases of ocular allergy. The first case was that of a man aged 60 who had been operated on for senile cataract. The operation and the postoperative period were uneventful. Drugs used before, during and after operation were cocaine, merbromin, procaine hydrochloride, physostigmine and atropine. A month later the second eye was operated on, and the procedure was interrupted several times, owing to the condition of the patient, who was perspiring profusely, with slow pulse and dyspnea, these symptoms having commenced after the retrobulbar injection of procaine. Allergy being suspected, 0.5 cc. of procaine hydrochloride was injected intradermally, causing development of the same symptoms. The second case was that of a man aged 21, with acute catarrhal conjunctivitis. No results were obtained with the classic therapy. Treatment was suspended for two days, and at the end of this period the allergic symptoms disappeared. Cocaine was suspected as the allergin.

M. E. ALVARO.

General Diseases

ARACHNODACTYLY (MARFAN'S SYNDROME) ASSOCIATED WITH ECTOPIA LENTIS. J. V. CASSADY and C. B. MCFARLAND, Am. J. Ophth. **30:** 469 (April) 1947.

Cassady and McFarland review the literature of Marfan's syndrome, emphasizing its hereditary and familial tendencies. They report a case with the usual characteristics, as well as a detached retina pulled loose by a dislocated lens and a pigmented, band-shaped corneal degeneration. The lens was removed, but vision was limited to light perception and projection. The fellow eye was blind from glaucoma.

W. S. Reese.

Extensive Symmetrical Cerebral Calcification and Chorioretinitis in Identical Twins (Toxoplasmosis?). K. H. Abbott and J. D. Camp, Bull. Los Angeles Neurol. Soc. **12**: 38 (March) 1947.

Abbott and Camp report observations on twin boys aged 11 years who were brought to the Mayo Clinic because of visual disturbances and disturbances of movement in the right extremities. The disturbances were more evident in the more severely affected of the two boys, who also had bilaterally symmetric, extensive, dense calcification in the cerebrum with minor involvement of the cerebellum. Both patients had extensive chorioretinitis, which was severer on one side, associated with retinal angiomatosis. Blood serum from each twin neutralized toxoplasma organisms. The pathogenesis and the histopathology of this syndrome—symmetric cerebral calcification, chorioretinitis with retinal angiomatosis and toxoplasmosis—are unknown. Although a degenerative process occurring in symmetric anomalies of vascular or heterotopic nervous tissue or both may be the causal factor, it is more plausible that the syndrome is due to an inflammatory process, probably consequent to chronic toxoplasmosis.

W. Zentmayer.

The Fundus in Cases of Hypertension in Which the Smithwick Method Was Used. M. Puig Solanes, Gac. méd. de México **77**: 16 (Feb.) 1947.

The author reaches the following conclusions:

1. During the first few weeks after the Smithwick operation in cases of hypertension, an increase in the narrowing of the retinal arterioles, which accentuates the "edematous" papilloretinal lesions, is observed.

2. Within a few months the angiospasm (localized constrictions) and the "edematous" lesions disappear, the tonic contraction (generalized uniform narrowing) of the arterioles remaining. These, according to investigators who have kept the patients under observation for years after operation, also tend to disappear in time.

3. The alterations in the retinal vessels in the patients after operation are independent of the effect produced by the operation on the arterial tension and the general health of the patient.

4. It is supposed that similar alterations occur in other circulatory regions of the organism, especially in the brain.

M. E. Alvaro.

General Pathology

Data on the Occurrence of Calcification in the Eye Tissues. M. Radnót, Brit. J. Ophth. **32**: 47 (Jan.) 1948.

The cases discussed in this study were those of so-called ribbon type degeneration. It was sought to find out what changes are present

in tissues of the eye other than the cornea, especially whether calcareous deposits occurred elsewhere. On the basis of this investigation, it is observed that when lime is deposited in the cornea in zonular opacity or in eyes injured in some other way, a calcareous deposit is also to be seen in other tissues of the eyeball. The article is well illustrated.

W. ZENTMAYER.

Glaucoma

ACUTE GLAUCOMA: A FOLLOW-UP STUDY. H. S. SUGAR, Am. J. Ophth. 30: 451 (April) 1947.

From a study of 45 patients with "primary" acute glaucoma followed over a period of six years, Sugar concludes that the inclusion of a description of the vascular reaction of the eye in the main diagnosis is unjustified, the various types of response constituting clinical phases of the same condition. He also concludes that miotics have the disadvantage of adding a congestive, angle-narrowing factor in a situation in which the angle is already anatomically too narrow. He suggests the use of a combination of miotics and vasoconstrictors.

W. S. REESE.

INDICATIONS FOR IRIDECTOMY IN HEMICYCLODIALYSIS. ANTONIO TORRES ESTRADE, Bol. Hosp. oftal. Ntra. Sra. de la Luz 3: 237 (Jan.-Feb.) 1947.

The author believes that iridectomy is a valuable aid in hemicyclodialysis, making the latter operation less dangerous and eliminating its complications. Iridectomy may be performed weeks before the hemicyclodialysis, or at the same operative session.

Iridectomy should be mandatory as the final stage of the operation in cases of hemorrhage and when abundant segregation of uveal pigment is present. Iridectomy combined with hemicyclodialysis is also indicated in cases of a shallow anterior chamber, in the slightly advanced stages of glaucoma, in cases of congestive glaucoma, in cases with degenerative lesions of the iris and in cases in which the general condition of the patient allows one to foresee inflammatory reactions during the postoperative period.

M. E. ALVARO.

Hygiene, Sociology, Education and History

OPHTHALMOLOGY DURING THE WAR AND IN THE FUTURE. S. DUKE-ELDER, Am. J. Ophth. 30: 1073 (Sept.) 1947.

In this address, presented at the eighty-second annual meeting of the American Ophthalmological Society, the author considers advances in chemotherapy, various aspects of physiology, evaluation of experimental opportunities, integration of research and responsibilities of the future.

W. S. REESE.

NEW YORK AS AN OPHTHALMOLOGICAL CENTER.. B. SAMUELS, Am. J. Ophth. 30: 1081 (Sept.) 1947.

This interesting account begins with the founding of the New York Eye Infirmary in 1820, around which revolved all matters concerned

with the eye. Outstanding ophthalmologists and various ophthalmologic institutions are mentioned as they fit into this history.

W. S. REESE.

Injuries

TREATMENT OF TRAUMATIC DIPLOPIA. J. C. NEELY, Brit. J. Ophth. **31**: 581 (Oct.) 1947.

The material for this lengthy dissertation was drawn from the records of patients who were seen by Neely at a military hospital for head injuries and at a Royal Air Force hospital. A complete analysis of each of the 55 cases is appended.

The following summary is given:

1. Traumatic diplopia is not an uncommon sequel to a head injury.

2. Diplopia is caused usually by a paresis, and not a paralysis, of an extraocular muscle.

3. In the majority of cases, the "closed" head injury, and not the penetrating head wound, is the cause of diplopia.

4. The vertically acting muscles are most often affected.

5. Injuries to the orbit tend to be overlooked, owing to the severity of other injuries, or masked by the swelling of the surrounding tissues.

6. The roentgenologic diagnosis of fracture of the floor of the orbit is difficult to make unless stereoscopic pictures are taken in the vertico-mental position of the head.

7. In cases of fractures involving the orbit, the restoration of the normal anatomic relation of the parts is of immediate importance.

8. The orbital floor can be built up by means of a bone inlay if immediate restoration has not been effected.

9. Well planned surgical procedures on the extraocular muscles, aided by orthoptic exercises, represent the best means of overcoming the residual diplopia and of restoring binocular single vision.

The article is illustrated with photographs of the patients' eyes in the fields of fixation, charts of the field of fixation and, in many cases, roentgenograms of the orbit and skull.

W. ZENTMAYER.

Lens

THE ACTION OF SULPHANILAMIDE ON RABBITS' LENSES IN VITRO. A. BAKKER, Brit. J. Ophth. **31**: 216 (April) 1947.

The perfusion culture method gave reliable information on the toxic action of chemicals. The present experiments showed that sulfanilamide has no injurious effect on rabbit lenses when the concentration is not raised above the level reached in normal therapeutic doses. Nevertheless, caution is advisable in using this drug. The author was told that in a 43 year old patient, with erysipelas of the face, who was treated with "prontosil" (the hydrochloride of 2,4-diaminoazobenzene-4-sulfonamide) for no less than four months there developed cataractous changes of capsular and subcapsular type in both lenses.

There was a striking difference between the behavior of the lenses of young and those of old animals. The younger the animals, the more their lenses were susceptible to the noxious influence of sulfanilamide.

W. ZENTMAYER.

CATARACT AFTER TETANY. R. GARCIA OCHOA and A. ETCHEMENDIGARAY, An. argent. de oftal. **7:7** (Jan.-March) 1946.

Tetany is not frequent, and cataract as a complication of tetany is even less so. A woman aged 41 had been treated for hyperthyroidism for three years, and at the end of this time the lower portion of the right thyroid gland was removed. On the third postoperative day an acute attack of tetany occurred, for which intravenous injections of calcium were given. Since the attacks continued as soon as injections were suspended, a graft of parathyroid tissue on each side of the trachea was performed. The tetany continued until four more grafts had been made. Thirteen months after the first symptoms of tetany, total, bilateral cataract, obviously correlated with the tetany, was noted. The pathogenesis of such cataracts is discussed. M. E. ALVARO.

Methods of Examination

MEASUREMENT OF RELATIVE EXOPHTHALMOS BY ROENTGENOGRAPHY. BENJAMIN FRIEDMAN, U. S. Nav. M. Bull. **45:** 482 (Sept.) 1945.

The patient lies on the x-ray table, with eyes looking straight upward; a contact glass carrying a small central lead dot is placed over each eye; the roentgen rays are directed from the foot of the table so that the central ray passes through the lead dots at an angle of 35 degrees with the table; the shadows of the lead dots fall on the film. If one eye protrudes more than the other, the dot over the relatively exophthalmic eye will be projected farther back than the dot over the less protruding eye. A method of positioning the eyes in space in such a manner as to eliminate sources of error is described. The measurements are precise and are in most cases less than the variations found in repeated readings with the exophthalmometer. They record relative, not absolute, exophthalmos. This method does not supplant instrumental exophthalmometry; the two methods should supplement and check each other. BENJAMIN FRIEDMAN.

PERIMETRIC CHARTS IN EQUIVALENT PROJECTION, ALLOWING A PLANOMETRIC DETERMINATION OF THE EXTENSION OF THE VISUAL FIELD. J. TEN DOESSCHATE, Ophthalmologica **113:** 257 (May) 1947.

In this study, the author attempts to project the visual field as recorded from the surface of a sphere on to a plane surface, that is, a perimetric chart. The problem is the same as that which has been studied for centuries by geographers and astronomers. The author discusses problems involved in detail and describes a perimetric chart in equivalent projection which allows a planometric determination of the area of the field of vision on the visual sphere. If C represents the relative part of the visual field (and of the retinal surface approximately) which is still physiologically active, then C equals

$$\frac{S}{So}$$

where S represents the surface of the visual field of the patient and So is the surface of the normal visual field. The author attempts, further, to describe the construction of a perimetric chart in which the area of the field is a measure of the active number of percipient retinal units. It is shown, however, that such a chart has no practical clinical value.

F. H. ADLER.

Neurology

DISEASES OF THE BRAIN AND OPTIC NERVE: CONCENTRIC RESTRICTION OF VISION FROM UNILATERAL CEREBRAL LESIONS. A. PATERSON, Tr. Ophth. Soc. U. Kingdom **64**: 115, 1944.

Concentric constriction of peripheral vision in the nonhemianopic half-fields arising from a unilateral lesion has frequently been observed in the past. Although the older neurologists believed that this syndrome had an organic basis, it is now usually considered to be of functional origin. Two cases presenting these field changes are reported. In both, sustained fixation was difficult. In the first case the patient sustained a unilateral tangential, through and through bullet wound; the entrance was in the right frontal region and the exit just in front of the tip of the right ear. As a result, there was a large intracerebral hemorrhage in the right cerebral hemisphere from rupture of a branch of the middle cerebral artery, giving rise to left hemianesthesia and hemiplegia. In the second case the diagnosis was that of cerebral thrombosis, either in a terminal branch of the middle cerebral artery in the region of the angular gyrus, and affecting in the main the optic radiation in its narrow part as it sweeps round the temporal horn, or, more probably, in the posterior cerebral artery, fairly far forward and affecting the subcortical connection of the angular gyrus. An explanation of these field changes is attempted. One factor may be the difficulty in sustained fixation. Two possible factors in this phenomenon are, first, a probable defect in oculomotor integration and, second, impairment of the visual attention process itself. Another factor may be that the test object fails to excite attention, or at least to evoke a perceptual response, until it approaches the region of central vision. Still another factor is dark adaptation, which was poor in both cases, as the luminosity of neither test object nor background is as a rule particularly high and some degree of dark adaptation almost certainly takes place during the test. The discrepancies between the results of perimetric and campimetric examinations are described: The fields are much more constricted on the screen than on the perimeter; this may be interpreted as a gross exaggeration of a normal phenomenon, namely, that peripheral acuity is better for a near object than for a distant one when both are arranged to subtend identical retinal angles and the illumination is likewise equated.

W. ZENTMAYER.

THE CENTRAL VISUAL FIELD AFTER OCCIPITAL LOBECTOMY. K. PORSAA, Acta ophth. **22**: 241, 1944.

The theory of bilateral macular representation in the cortex has been questioned by many investigators. One of the chief arguments against it is the frequent occurrence of occipital hemianopsias without macular sparing—a fact which any acceptable theory must take into account. Horrax and Putnam, for instance, found macular sparing in only 74 per cent of cases of hemianopsia resulting from uncomplicated occipital tumors, and Allen, in 39 per cent.

After a brief consideration of other theories that have been advanced to explain sparing of the macula, the author reports 5 cases in which

an occipital lobectomy was performed without injury to the corpus callosum or involvement of the temporal lobe. The fields of vision in all 5 cases were taken after the patient had staged a good recovery. In all cases there was a sharply defined hemianopsia with bisection of the macula. The author believes that these cases show more clearly than any previous investigative studies that there can be no bilateral representation of the macula in the cortex. O. P. PERKINS.

Ocular Muscles

TESTS FOR HETEROPHORIA. R. G. SCOBEE and E. L. GREEN, Am. J. Ophth. **30:** 436 (April) 1947.

Scobee and Green conclude from tests on the eyes of cadets of the air corps that Maddox rod tests give results sufficiently like those with the screen and parallax test to be used as a routine. They recommend that a white rod be used, without screening, and that it may be placed before the dominant or the nondominant eye, according to routine.

W. S. REESE.

SOME OBSERVATIONS ON THE SURGICAL TREATMENT OF THE EXTRAOCULAR MUSCLES. A. DEH. PRANGEN, Am. J. Ophth. **30:** 1161 (Sept.) 1947.

Prangen expresses his individual views on surgical treatment of the extraocular muscles and refers to his technic in and preference for various operative procedures.

W. S. REESE.

ORTHOPTIC TREATMENT IN CONVERGENCE INSUFFICIENCY. C. E. DAVIES, Canad. M. A. J. **55:** 47, 1946.

Davies has found that convergence insufficiency bears no relation to refraction and is not cured by correction of refractive errors, except in some cases of undercorrected myopia and overcorrected hypermetropia. The incorporation of prisms in a prescription will not constitute a cure, as prisms do not produce the development of a convergence reserve. In the author's experience, operation has not proved satisfactory in cases of convergence insufficiency, as the condition is functional. In extreme cases, however, it may go on to heterophoria. Repeated convergence on a test object is a quick and accurate test for convergence insufficiency. Convergence insufficiency with esophoria was found to take the longest time to correct because correct abduction had to be taught as well as adduction, i. e., divergence insufficiency.

W. ZENTMAYER.

Operations

USE OF DEAD TISSUE IN OPHTHALMIC REPAIR. A. MAGITOT, Ann. d'ocul. **180:** 146 (March) 1947.

The author discusses the use of both living and preserved tissue as transplant material in the human body. In most instances the donor material is replaced by cells from the host.

Reference is made to the use of calf's cartilage and its perichondrium for implantation in Tenon's capsule after enucleation. Recently the author has used the head of the femur from a dog. It is stripped of all cartilage and then preserved in 60 per cent alcohol. After operation there is the minimum reaction to the transplant. With the availability of such material, there is no reason for using inert implants in the socket. One should also pay attention to the cosmetic appearance of the patient. The sunken upper lid can be improved by placing a suitable plastic or cartilage in the upper lid under the brow. P. R. McDONALD.

USE OF THROMBIN-GELATIN SPONGES IN OPHTHALMIC SURGERY. CRUT and A. DOLLFUS, Bull. Soc. d'opht. de Paris, March-April 1947, p. 126.

The authors used thrombin-gelatin sponges in 4 cases of surgical procedures for ocular conditions, viz., staphyloma of the cornea, painful absolute glaucoma with trophic keratitis, exenteration of the orbit and painful absolute glaucoma with thrombosis of the central retinal vein. In all cases the bleeding was stopped very quickly. The length of the duration of each operation was definitely shortened. It is necessary to follow the recommended technic for best results in the use of this new method of controlling bleeding. L. L. MAYER.

Orbit, Eyeball and Accessory Sinuses

THE ROLE OF THE DIENCEPHALON IN REGULATING OCULAR TENSION. E. SCHMERL and B. STEINBERG, Am. J. Ophth. **31**: 155 (Feb.) 1948.

Schmerl and Steinberg conclude that it may be postulated, on the basis of experiments performed under the conditions described, that the diencephalon contains a center or centers which exercise a regulating control of ocular tension. The experiments also suggest an instability of the diencephalic center or centers in glaucomatous animals.

W. S. REESE.

NONINFLAMMATORY EXOPHTHALMOS. ESTEBEN ADROGUE and FEDERAICO C. CERBONI, Arch. de oftal. de Buenos Aires **23**: 1 (Jan.-March) 1947.

The authors discuss exophthalmias of the noninflammatory types.

Definition.—Exophthalmos means a displacement of the eye forward, out of the normal anatomic position it occupies in the orbit. Anatomic and physiologic details are given.

Pathogenesis.—The pathogenic factors are: (1) a decrease in the forces which maintain the globe in its position in the orbit, (2) an increase in the quantity of blood in the orbit and (3) an increase of the orbital contents, due to neoplasms.

Semeiologic Considerations.—The authors classify the various types of exophthalmos on the basis of the following factors: direction; evolution; reducibility; involvement of motility; palpability and nonpalpa-

bility; alterations in the fundus, vision or visual fields; associated local symptoms; roentgenographic symptoms; diagnostic proof, and general clinical data, such as age, frequency, sex and localization.

Therapy.—The treatment of noninflammatory exophthalmos depends on the cause and is usually surgical; therefore, only the types which respond to surgical treatment are considered in this article. Various types of operations are discussed. M. E. ALVARO.

Retina and Optic Nerve

PAPILLEDEMA AND PAPILLITIS. M. CHAMLIN, Am. J. Ophth. **30**: 741 (June) 1947.

Chamlin discusses papilledema and papillitis from the standpoint of ophthalmoscopic findings, visual acuity and visual fields. He concludes that studies of the central fields are of paramount importance in the differentiation of these two conditions. W. S. REESE.

EXPERIMENTAL STUDIES IN RETROBULBAR NEURITIS. P. J. LEINFELDER and W. A. ROBBIE, Am. J. Ophth. **30**: 1135 (Sept.) 1947.

Despite the fact that the groups of animals with deficiencies in B complex and in thiamine were reduced to extreme degrees of malnutrition, in none of their experiments did Leinfelder and Robbie find significant degeneration in the optic nerves. They discuss the results of these experiments in their significance and mention certain inadequacies of the present experimental methods. W. S. REESE.

RETINAL HEMORRHAGES PRECEDING PAPILLEDEMA. G. OFFRET, Bull. Soc. d'opht. de Paris, November-December 1946, p. 65.

Attention to retinal hemorrhages, in 2 patients with vasomotor reactions, is focused on the development of papilledema. Both patients had intracranial lesions, and the author believes that the retinal hemorrhages are an early phase in the development of edema of the nerve head. L. L. MAYER.

HOLE IN THE MACULA AFTER A SINGLE HEMORRHAGE. A. B. RECA, An. argent. de oftal. **7**: 10 (Jan.-March) 1946.

A woman aged 29 years complained of a sudden decrease in visual acuity in the left eye. The optic disk appeared to be normal; the arteries were thin and somewhat rigid. Along the course of the large veins small hemorrhages were visible. A large hemorrhage occupied the entire region of the macula. Twenty days after the first examination the hemorrhage had disappeared, leaving in its place an oval hole. The bottom of the depression was brownish, with large, brilliant dots, possibly due to cellular disintegration. The author reaches the following conclusion: Owing to the absence of a history of earlier ocular disease, the brownish color of the lesion and the presence of the large, brilliant spots, as well as the permanent character of the lesion, the lesion may be classified as a "traumatic hole of the macula." M. E. ALVARO.

MIGRATING CILIARY NODULES ON THE RETINA. D. DÍAZ DOMINGUEZ, Arch. Soc. oftal. hispano-am. **6**: 265 (March) 1946.

Díaz Dominguez describes his observations in the case of a woman aged 62 who presented signs of bilateral iridocyclitis. There were ciliary injection and pain on pressure in both eyes. Examination revealed keratic precipitates on Descemet's membrane and pigmented deposits on the anterior surface of both crystalline lenses and floating cells in the vitreous. The fundi were normal on the first examination. Four days later, however, the author observed in the lower part of each fundus, toward the periphery, two small, whitish, prominent spots, which he interpreted as two foci of choroiditis. The patient felt better under treatment and disappeared, to come back two years later with recurrence of symptoms. This time the author observed two new nodules in the lowermost part of the fundus in the right eye, in the vicinity of those seen two years before. This time he could see that the well limited, grayish white nodules were located on the surface of the retina. Because of their location on the retina, and in the most dependent portion of the fundus, the observer concluded that these formations had dropped off from the ciliary body, to be lodged in the retina.

Similar cases had been described before by Szily and Krückmann, but the author is not in accord with Szily in his assertion that the condition occurs only with tuberculous iridocyclitis. He is of the belief that, as in his case, in which the condition was proved not to be tuberculous, these migrating nodules may be associated with any type of anterior uveitis.

H. F. CARRASQUILLO.

Tumors

CANCER OF EYELID TREATED BY RADIATION, WITH CONSIDERATION OF IRRADIATION CATARACT. H. B. HUNT, Am. J. Roentgenol. **57**: 160 (Feb.) 1947.

The survey presented by Hunt is based on a study of 100 cases selected from 134 occurring from 1930 to 1946. Carcinoma of the eyelid is a disease of the older age group, three fourths of the patients being past 60 years of age. Men are slightly more susceptible than women. Four fifths of the lesions are located along the lower lid or about the inner canthus. Basal cell carcinoma represents three fourths of the neoplasms of the eyelid, and this lesion is usually of slow growth. Squamous cell carcinoma of the eyelid, although not common, is a more serious lesion, shows greater local invasion and frequently metastasizes to the parotid or the submaxillary gland. Cancer of the eyelid can be as effectively controlled by fractionated roentgen therapy as by surface application of radium. Careful fulguration is the treatment of choice in the removal of benign moles or papillomas. Surgical ablation of a large, elevated carcinoma of the eyelid prior to roentgen therapy permits more effective treatment of its base, with less mass irradiation of the eyeball and other adjacent, nondiseased, tissues by both primary and scattered rays. In 4 of the 100 cases reviewed, death occurred from cancer of the eyelid during the past fifteen years. Therapeutic failures are the result of advanced and inaccessible disease, impairment of the tumor bed by prior inadequate therapy, insufficient or uneven dosage, incomplete marginal coverage of the lesion and inadequate follow-up observation of the patient. Superficial roentgen therapy is effective in

eradication of cancer of the eyelid, with maximal preservation of the uninvolved tissues and with minimal injury to the eye when properly protected by an eye shield. J. A. M. A. (W. ZENTMAYER).

MALIGNANT RETICULAR TUMORS OF THE FACE. J. DELARNE and G. OFFRET, Bull. Soc. d'opht. de Paris, November-December 1946, p. 103.

Deep tumors of the face as noted by the clinician are epitheliomas of the bony cavities and osseous sarcomas.

Tumors were observed in the orbit in 10 cases; in the nasal fossa, in 1 case; in the inferior maxilla, in 2 cases; in the frontomalar region, in 1 case, and in the superior maxilla, in 1 case.

The authors divide the reticular tumors as follows: (1) indifferent reticulosarcoma, (2) reticuloangioendotheliosarcoma and (3) lymphoreticulosarcoma.

The authors discuss the various tumors in respect to age of appearance, type and relation to other disease processes, such as mycosis fungoides, either local or general. They believe that the Mikulicz tumor is a separate entity. L. L. MAYER.

SPONTANEOUS CYST OF THE IRIS. H. MARBACK, Arq. brasil. de oftal. 9: 1 (Feb.) 1946.

A woman aged 27 complained of a small spot on the iris of the right eye. This spot had not increased in size or changed color. There was no history of trauma. Examination revealed a small tumor in the upper temporal quadrant of the iris, and in the anterior chamber there was a small cyst between the anterior surface of the iris and the posterior surface of the cornea. Surgical removal of the cyst was recommended, but permission was refused by the patient. Examination made two and a half years later showed no change in the size of the cyst.

M. E. ALVARO.

CHOROID METASTASES IN CHORIONEPITHELIOMA [CHORIONIC CARCINOMA] OF THE TESTICLE. E. GODTFREDSEN, Acta ophth. 22: 300, 1944.

In a youth aged 18, a tumor of the right testis necessitated semicastration. Microscopic examination of the growth revealed chorionic carcinoma. Shortly after the operation, choroidal, cerebral and pulmonary metastases occurred, ending in the patient's death twelve months after the onset of symptoms. All the metastatic growths were of the same type as the original tumor. O. P. PERKINS.

ON THE FREQUENCY OF SECONDARY CARCINOMAS IN THE CHOROID. E. GODTFREDSEN, Acta ophth. 22: 394, 1944.

In a series of about 8,000 patients with cancer attending the radium center and the Finsen Institute, in Copenhagen, choroidal metastases developed in 6. Such metastases occur with equal frequency with pulmonary cancer and with cancer of the breast. Furthermore, metastatic tumors constitute between one third and one half of the total number of intraocular tumors occurring in Denmark. O. P. PERKINS.

Uvea

THE INFLUENCE OF HYPERSENSITIVITY ON ENDOGENOUS UVEAL DISEASE. A. C. WOODS, Am. J. Ophth. **30**: 257 (March) 1947.

In this, the Jackson Memorial Lecture, Woods discusses the influence of hypersensitivity on endogenous uveal disease. The clinical difference between two types of uveal disease, nongranulomatous and granulomatous, are pointed out. Both types are dependent on invasion of the eye, at one time or another, by living bacteria; but the pathogenesis and character of the lesions in these two types of uveal disease appear to be quite different. In the nongranulomatous type, the primary invasion of the eye is probably by organisms either of low virulence or in small numbers. The result is that they are destroyed by the normal bactericidal action of the ocular fluids. This primary invasion produces insignificant lesions or no lesions at all, but it does produce a local hypersensitivity of the ocular tissues to the bacterial protein or to the soluble bacterial products. This hypersensitivity may be of the bacterial type, or of both the anaphylactic and the bacterial type. When the bacterial antigens again reach the eye, either through reinfection or absorption from an infected focus, or even a normal cutaneous surface or mucous membrane, there results a hypersensitive reaction in the eye. This reaction is produced either by organisms which do not proliferate or by their bacterial products. In either event, the reaction is essentially an evanescent one and is characterized by an intense vascular congestion and a minimum of tissue damage—the picture of a nongranulomatous uveitis.

In the granulomatous type of uveitis, the mechanism is quite different. The organisms reaching the eye are not destroyed but remain viable in the ocular tissues, and, by their presence, proliferation and inherent toxicity, produce local lesions in the eye. The character of the resulting lesion is profoundly modified and influenced by the factors of local hypersensitivity and general immunity. The proliferation of the organisms in the eye produces a local hypersensitivity to the bacterial products. This hypersensitivity is of the bacterial type, and a reaction between the hypersensitive tissue and the bacterial products may thereafter result. If the proliferation of the bacteria is not restrained by the forces of immunity, this hypersensitive reaction will be progressive, characterized by inflammation, caseation, necrosis, tissue destruction and often a compensatory overgrowth of granulomatous tissue. If, however, there is present either a natural or an acquired resistance to the infection, the proliferation of the bacteria is restrained, and the reaction is minimal.

W. ZENTMAYER.

Therapeutics

LOCAL PENICILLIN THERAPY OF HYPOPYON FORMATION, WITH SPECIAL REFERENCE TO USE OF SUBCONJUNCTIVAL INJECTION. A. SORSBY and H. REED, Brit. J. Ophth. **31**: 528 (Sept.) 1947.

Results of treatment, chiefly with penicillin, are recorded for 66 patients with hypopyon.

This series included 39 patients with infected corneal ulcer; 18 of these were treated with subconjunctival injections of penicillin in doses of 50,000 units, with or without the application of penicillin ointment

in concentrations of 25,000 to 100,000 units per gram of base. Other methods of local penicillin therapy were employed with 12 patients. Two patients received oral treatment with sulfonamide drugs, and 4 others, local penicillin therapy combined with general sulfonamide therapy. For 3 patients, general sulfonamide therapy was used when subconjunctival injections of penicillin proved inadequate.

Twelve patients with hypopyon formation associated with herpetic or neuropathic corneal lesions were treated with various applications of penicillin locally, with or without general sulfonamide therapy. There were also 5 patients with long-standing glaucoma showing hypopyon as a complication. A final group of 10 patients presented 13 instances of hypopyon iritis.

Infected corneal ulcers responded well to treatment. Hypopyon seen in cases of herpetic or neuropathic keratitis gave no response. Hypopyon iritis appeared to require no treatment other than atropine.

A detailed analysis of the cases of infected corneal ulcer with hypopyon in which various types of penicillin therapy were used shows that subconjunctival injection is the method of choice. This therapy was successful in 18 of 21 cases. The mode of treatment is described. It consists essentially in twelve to sixteen subconjunctival injections each of 50,000 units of penicillin (dissolved in 0.25 cc. of 2 per cent procaine hydrochloride and 0.25 cc. of epinephrine hydrochloride [1:1,000]) at intervals of six hours, followed by the instillation of penicillin ointment in a concentration of 100,000 units per gram every four hours.

The following method of preparation of the penicillin for subconjunctival injection was employed: Into an ampule containing 100,000 units of white crystalline penicillin, 0.5 cc. of 2 per cent procaine hydrochloride and 0.5 cc. of epinephrine hydrochloride (1:1,000) are injected. Five-tenths cubic centimeter is now withdrawn and injected subconjunctivally.

W. ZENTMAYER.

USE OF CHOLINE IN OPHTHALMOLOGY. M. MARIN AMAT, Arch. Soc. de oftal. hispano-am. **6:** 33 (Jan.) 1946.

The use of choline derivatives in the treatment of glaucoma is well known. The author stresses the value of this drug in the treatment of the following ocular conditions: (1) serpiginous ulcer of the cornea, (2) leukoma of the cornea, (3) purulent iritis consequent to corneoscleral trephination and trauma, (4) incipient panophthalmitis, (5) suppurating socket after enucleation, (6) phlegmonous inflammation after operations for strabismus, (7) chronic dacryocystitis and (8) cholesterol infiltration of the cornea.

A 1 per cent solution of choline with merbromin is instilled. A number of cases are reported in which the disappearance of leukoma with the use of instillations of choline was dramatic.

Reference is made to the oral use of the drug by other authors in the treatment of retinal tuberculosis.

H. F. CARRASQUILLO.

Toxic Amblyopia

MODIFICATIONS OF THE CRITICAL FUSION FREQUENCY IN THE COURSE OF TOBACCO AMBLYOPIA. F. ROUSSEL and R. WEEKERS, Ophthalmologica **113:** 215 (April) 1947.

The authors used a method for determining the critical fusion frequency, which they have previously described, in a patient with tobacco amblyopia. They found a lessening of the critical fusion frequency in the region of the fixation point and the blindspot which parallels the extension and density of the centrocecal scotoma. Changes in the frequency of fusion paralleled the improvement in the condition, and the authors state that this is a sensitive method by which to follow the course of the disease, as the lessening of the frequency of fusion can still be demonstrated when the visual acuity has returned to normal and campimetric studies show no further field defects. It is not certain as yet whether these changes in the frequency of fusion are pathognomonic of tobacco amblyopia.

F. H. ADLER.

PATHOGENESIS OF THE LAESIO GANGLII VESICULI OPTICI. J. DE RUYTER, Ophthalmologica **113:** 276 (May) 1947.

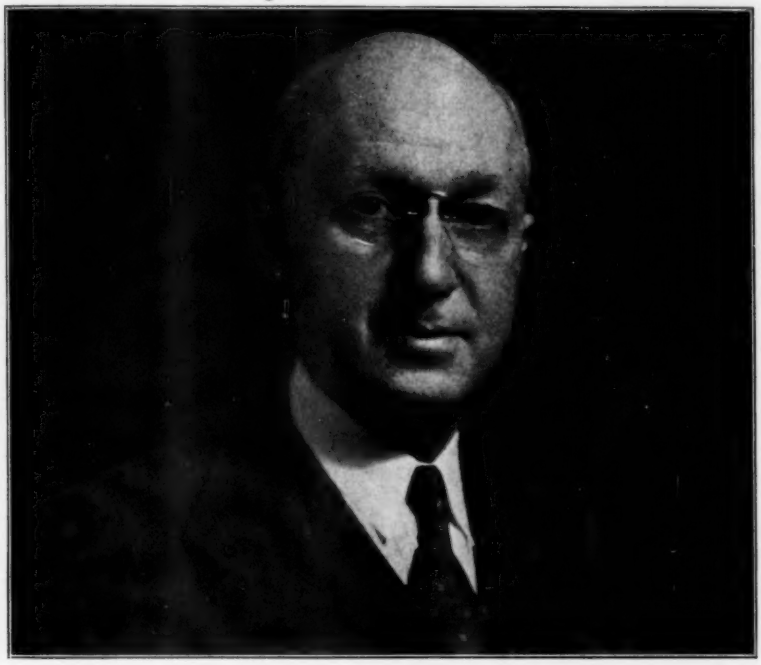
The author calls attention to the fact that in methyl alcohol intoxication the disease process begins in the ganglion cells of the retina and not in the optic nerve fibers. He uses the awkward term "laesio ganglii vesiculi optici" because the optic nerve is not a true peripheral nerve and the disease process should, therefore, not be called a neuritis. He believes that the observations of Burki and Schmid (*Ophthalmologica* **105:** 165 and 121, 1943) throw light on the pathogenesis of methyl alcohol poisoning and tabetic primary atrophy of the optic nerve, which also begins in the ganglion cells of the retina. These authors found that only the layer of multipolar cells in the retina contains ascorbic acid. de Ruyter considers that this finding accounts for the involvement of the ganglion cells, since these cells are in an exceptional position as regards the chain of redox reactions governing cellular respiration. Any poisons which impede these redox reactions, in which the vitamins, such as ascorbic acid, are involved, would affect these cells first.

F. H. ADLER.

Obituaries

H. MAXWELL LANGDON, M.D.
1876-1947

H. Maxwell Langdon was born in Philadelphia, June 21, 1876, the son of Giles Maxwell Langdon and Frances Jane Smith Langdon. He received his preparatory education at the Rugby Preparatory School; for a time he attended the Collegiate Department of the University of Pennsylvania and received his medical degree at the University of Pennsylvania in 1901. His basic education in ophthalmology was



H. MAXWELL LANGDON, M.D.
1876-1947

acquired at the Royal Ophthalmic Hospital (Moorfields), London, England. At various times, he served as ophthalmologist to the Howard, Children's, Orthopedic, University of Pennsylvania and Presbyterian Hospitals. He was a fellow of the American Medical Association, a member of his county and state medical societies and a fellow of the College of Physicians of Philadelphia, and at one time chairman of the Section on Ophthalmology of the College. He was professor of

ophthalmology in the Graduate School of Medicine of the university, teaching the subject of refraction. He was elected a fellow of the American Ophthalmological Society in 1912. His college fraternity was the Phi Kappa Psi and his medical fraternity the Alpha Mu Pi Omega. He was active in the St. Andrews and in the Pennsylvania Historical Society. He worshiped in the Presbyterian Church.

Dr. Langdon did not contribute largely to the literature, but several of his contributions were notable. He early became interested in the study of the light sense and, together with Mr. H. E. Ives, devised a practical photometer. In 1938 Dr. Langdon reported on the successful use of the thermophore in selected cases of detachment of the retina. His lectures on refraction were delivered tersely and fluently, and were often punctuated by wit and apt anecdotes. In discussions he was outspoken, at times critical and usually enlivening and enlightening. He was widely read, being particularly interested in English and early American colonial history, the events of which he could readily recall with remarkable detail. One of his hobbies was the collection of early prints.

On Nov. 29, 1905 he married Ethel Hancock. He is survived by his wife and daughter, Charlotte.

For many years, Dr. Langdon's activities were restricted by distressing angina, and his death came suddenly from coronary thrombosis, while he was returning to his home in Haverford, Pa., from a vacation in Portsmouth, N. H.

WILLIAM ZENTMAYER, M.D.

Book Reviews

Intracranial Tumors. Second edition. By Percival Bailey, M.D. Price, $10.50. Pp. 478, with 16 illustrations. Springfield, Ill.: Charles C Thomas, Publisher, 1948.

A second edition has permitted Dr. Bailey to correct and bring up to date his well known book on intracranial tumors. A brief atlas of roentgen photographs has been added. Ventriculography and Moniz' method of arteriography are carefully described, as, according to the author, they have greatly increased knowledge of the pathologic nature of a cerebral growth. There is also an excellent study of the hypothalamus, a region of the brain which is gaining in ophthalmologic interest. The importance in diagnosis of the presence of a nonfebrile, steadily increasing alteration in nervous function is emphasized, and this particularly appeals to the ophthalmic specialist, as lesions of the optic pathways are easily open to examination. There is an excellent description of hypophysial tumors, meningiomas and aneurysms, which are all lesions of the most frequent importance to the practicing ophthalmologist.

The text is delightfully clear, and there are no illustrations on annoyingly glossy paper. The ophthalmologist will find this an admirable book of reference.

ARNOLD KNAPP.

A Short History of Ophthalmology. Second Edition. By Arnold Sorsby, M.D., F.R.C.S. Price, 8s.6d. Pp. 103, with 7 illustrations. London: Staples Press, 1948.

When the author brought out the first edition of this work in 1933, he wrote as follows: "No attempt has been made to trace the growth of ophthalmology as an organic whole, phase by phase. It was thought more expedient to trace separately the course of the main streams of development." This plan has been left undisturbed in the second edition and has been admirably carried out. In his introduction, he has traced the development of general ophthalmologic knowledge from the time of Hammurabi through the Greek, Arabian, Medieval and Modern Ages. He then discusses the development of the anatomic, physiologic and pathologic knowledge from earliest historical times to the present. Subsequent chapters deal with cataract, glaucoma, therapeutics, spectacles and the ophthalmoscope. The book closes with a chapter on ophthalmology in the British Isles.

It is difficult to review this somewhat condensed type of work, but certain statements can be repeated to illustrate the interest and fascination aroused by reading it. It is entertaining to read that the Babylonians practiced couching for cataract; that the Egyptians knew of most diseases of the lids, from chalazion to dacryocystitis; that Roger Bacon wrote of convex lenses for presbyopia, and that da Vinci "either realized or came near to realizing" the principle of the camera obscura as applied to the eye. Here one finds the earliest anatomic drawing of the eye (Hünain ibn Is-hâq) and learns with surprise

the soundness of some of Hippocrates' and Galen's observations. The essential feature of glaucoma—hypertension—is generally thought to have been recognized in 1840, but Sorsby quotes Banister (1622) as "rubbing upon the eie-lids" to find if the "eye be growne more solid and hard than naturally it should be." The magnet was used to remove foreign bodies from the eye as early as 1627, and the first tattooing of the cornea was performed by Galen. Of interest (in view of contrary opinions so long and widely held) is Sorsby's contention that the Chinese learned about spectacles from the Europeans by way of Malacca. Glasses were certainly mentioned—and the sources are quoted—in 1299 and 1305. In fact, painters working in the fourteenth century endowed even biblical figures with these accessories.

These excerpts may serve to indicate to the potential reader that he should obtain this little book. I am sure that he will enjoy it.

G. M. BRUCE, M.D.

Bulletin of the Ophthalmological Society of Egypt. Volume XXXV. Pp. 196. Cairo, Egypt: Imprimerie Misr, 1948.

This bulletin brings a report of the proceedings of the Ophthalmological Society of Egypt during its thirty-ninth session, in 1942. Dr. Mohammed Mustafa El Bakry was president, and Dr. Mohammed Khalil, secretary. In addition to the president's address, the principal subject of discussion is syphilis of the eye. The other contributions cover a wide range of clinical features and include an illustrated article by Dr. Rowland P. Wilson, entitled "The Histopathology and Significance of Bulbar Follicles." The author concludes that the bulbar follicles are not trachoma follicles in the ordinary sense of the word but are lymph nodules formed *de novo* in the conjunctiva.

ARNOLD KNAPP.